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ABSTRACTS OF WORLD MEDICINE

UNDER THE DIRECTION OF

HUGH CLEGG, M.A., M.D., F.R.C.P., Editor, *BRITISH MEDICAL JOURNAL*

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This journal is planned to provide the reader with a selection of abstracts of the more important articles appearing in medical periodicals published in different parts of the world. Comment by the abstracter, when thought necessary, is inserted between square brackets, usually at the end of an abstract. In some instances only the titles of articles are provided.

The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals* and in *World Medical Periodicals*. The titles of articles from foreign journals are translated into English.

This journal is essentially a guide to work in progress in the world's medical centres. No abstract can be regarded as a substitute for the article abstracted. For complete information the original article must be consulted. Our aim is to give the reader sufficient details in an abstract to enable him to judge whether the original is, for him, worth reading in full.

The abstracts are grouped in broad classifications and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together under the same heading. The specialist will, it is hoped, learn from this journal of work done in other fields as well as in his own. The general practitioner will be able to keep abreast of modern knowledge in the various specialties. The representation in one journal of the several aspects of Medicine will, it is believed, give an integrated picture of the whole, necessary in this age of specialization.

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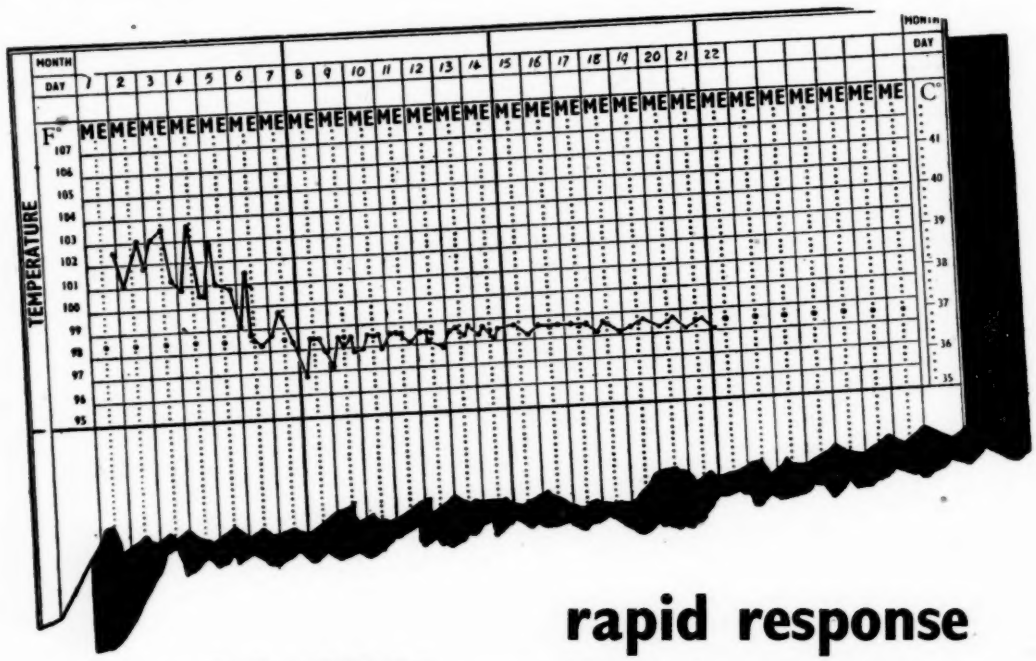

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ABSTRACTS OF WORLD MEDICINE

VOL. 16 No. 5 NOVEMBER, 1954

Pathology

EXPERIMENTAL PATHOLOGY

1206. **Pathogenesis of Bronchiectasis. Experimental Study and Anatomic Findings**
O. C. CROXATTO and A. LANARI. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **27**, 514–528, May, 1954. 7 figs., 31 refs.

As a contribution to the elucidation of the pathogenesis of bronchiectasis, the authors, working at the University of Buenos Aires, studied the changes occurring in the lungs of experimental animals during the development of bronchiectasis following obstruction of a bronchus. In 70 anaesthetized dogs the left bronchus was ligated and the animals killed at varying intervals ranging from a few hours to 6 months, after operation. Several of the dogs were subjected to a second operation at which one lobe of the lung and the bronchial stricture were removed, the lumen was re-established by anastomosis or insertion of a tube, and the remaining lobe re-expanded. Only 52 of the animals developed bronchial dilatation following bronchial ligation, it having proved impossible to produce total bronchial stenosis in the remainder.

Bronchial dilatation became apparent to the naked eye as early as 6 days after the operation. The earliest phenomenon was reabsorption of air from the respiratory parenchyma and bronchi. Mucus continued to be secreted by the bronchial glands and goblet cells and eventually dilated the bronchus (" mucous bronchodilatation "). After 2 months no further secretion of mucus took place, the intrabronchial pressure having become sufficient to produce compression of the acini. The final state was the formation of connective tissue and bronchiolar obstruction. Further study on re-operated animals and human lung specimens suggested the possibility that mucous bronchodilatation may, once the bronchus becomes recanalized, either disappear early, or later develop into bronchiectasis as a result of the bronchiolar obstruction or as a consequence of a co-existing bronchial or pulmonary infection.

A. I. Suchett-Kaye

1207. **The Erythropoietic Effect of Urine and Plasma of Repeatedly Bled Rabbits**
G. HODGSON and J. TOHÁ. *Blood* [*Blood*] **9**, 299–309, April, 1954. 4 figs., 36 refs.

In experiments carried out at the University of Concepción, Chile, support was obtained for the view that the primary stimulus for erythropoiesis is humoral. Plasma or urine from rabbits with post-haemorrhagic anaemia was injected into normal or into similarly anaemic rabbits. It was found that the reticulocyte response was greater after injections of plasma from anaemic rabbits than after injections of normal rabbit plasma, and that haemoglobin regeneration was accelerated by injections of urine from rabbits rendered anaemic by a " standard " haemorrhage. Evidence was found for the presence of at least two such erythropoietins—one in the blood of rabbits which had been bled and rabbits with anaemia induced by administration of phenylhydrazine, and the other in the blood of rabbits made anaemic by extracts of *Allium scorodoprasum* and rabbits rendered polycythaemic by exposure to low barometric pressure. Reference is made to the original observations of Carnot and Deflandre (*C.R. Acad. Sci.* (*Paris*), 1906, **143**, 384) [but the failure of their preparation to have therapeutic results in man is not explained].

A. Piney

1208. **The Lysis of Intravascular Thrombi in Rabbits with Human Plasmin (Fibrinolysin)**
C. E. GROSSI, E. E. CLIFFTON, and D. A. CANNAMELA. *Blood* [*Blood*] **9**, 310–320, April, 1954. 10 figs., 30 refs.

The effect of plasmin (fibrolysin), obtained from Fraction III of human plasma, on experimentally induced thrombosis is described in this paper from the Sloan-Kettering Institute and Memorial Center for Cancer and Allied Diseases, New York. Thrombosis was induced in the marginal vein of the rabbit's ear by injection of either thrombin or sodium morrhuate. Plasmin was then injected into a vein in the opposite ear at varying intervals after production of the thrombus, the average amount of plasmin given being 15 ml. per kg. body weight. Lysis of the clot occurred about one hour after the start of treatment, although in a small proportion of the animals it was incomplete. The wide variation in the fibrinolysin–antifibrinolysin systems of different animals is stressed.

A. Piney

1209. **The Role of the Nervous System in the Regulation of the Number of Leucocytes in the Peripheral Blood.** (Роль нервной системы в регуляции количества лейкоцитов периферической крови)
N. M. NIKOLAEV. *Клиническая Медицина* [*Klin. Med.* (*Mosk.*)] **32**, 31–37, Feb., 1954. 9 refs.

The author's thesis in this article is that blood formation is due to activation of the cells of the reticulo-endothelial system under the regulating influence of the

cerebral cortex. In considering the cell content of the peripheral blood, two processes have to be taken into consideration, namely, the production of cells and their distribution. These, the author holds, cannot both be due to one and the same mechanism. The present investigation is concerned only with the distribution of the cells.

In experiments on 15 puppies, 18 rabbits, and 18 guinea-pigs the animals were subjected to light and to deep narcosis, and the effects of this and of further stimuli on the leucocyte content of the peripheral blood were observed. Light narcosis was produced by giving 0·2 g. of barbitone sodium per kg. body weight, while deep narcosis was induced with 0·2 g. of amylobarbitone sodium per kg. body weight, with or without scopolamine or morphine by injection. It is stated that barbitone sodium acts predominantly on the cerebral cortex with relatively slight effect on the subcortical centres, whereas the deeper narcosis causes deep depression of both cortex and subcortex. Thus the influence of these centres could be observed separately. Light narcosis caused leucopenia in 11 of the 15 puppies and leucocytosis in the mature rabbits and guinea-pigs. Deep narcosis, on the other hand, caused leucopenia in 13 of 18 animals and a definite leucocytosis in only one. The author cites the work of Bayabdurov, who showed that leucocytosis occurred in animals after decerebration. The conclusion drawn from this experiment is that stimulation of the subcortical centres produces leucocytosis in the peripheral blood, but that if they, along with the cortex, are inhibited by a narcotic drug, leucopenia results.

The influence of cortical stimulation with caffeine and adrenaline was next studied. This produced a leucocytosis [but the number of animals affected is not given]. More striking were the results of experiments in which unnarcotized animals were subjected to emotional stimuli, chiefly in the form of threats. Some responded to these in an aggressive manner, whereas others were passive; the former were found to have a leucocytosis, while the others showed a leucopenia [again no numbers are given]. The conclusion drawn is that animals in which stimulation is the predominant mode of cortical activity form the first group, while those with an inhibitory tendency respond by the development of leucopenia.

In another series of experiments, after a preliminary blood estimation animals were subjected to laparotomy and the peritoneum swabbed with a 50% solution of turpentine. This caused dilatation of the mesenteric vessels, and leucopenia followed; but if 10 ml. of a 1% solution of procaine hydrochloride was previously injected intravenously, no leucopenia took place. Thus, the author concludes, the afferent path of these reflexes is formed by the sympathetic fibres from the vascular receptors, and he suggests that this explains the occurrence of leucopenia in the enteric fevers.

Finally, investigations were made on patients divided in two groups, the first consisting of children with nervous irritability and emotional instability due to trauma or war strain, and the second of adults who had developed severe reactions to *x*-ray therapy, with asthenia, loss of appetite, and nausea or vomiting. Of the children in the first group, a fasting leucocytosis was found in 18 out of 40 cases, and in 12 this persisted all day and during physiological sleep; injection of adrenaline raised still further the number of leucocytes. In the second group leucopenia was present, and injection of adrenaline was ineffective in producing any marked leucocytic response. [No marrow examinations were apparently performed to exclude damage to the haematopoietic tissue.]

The author's general conclusions are as follows. (1) Stimulation of both the cerebral cortex and of the subcortical centres causes leucocytosis. (2) Inhibition of the cortex with diminished cortical influence on the subcortical centres also causes leucocytosis. (3) Inhibition both of the cortex and of the subcortical centres leads to leucopenia. The author emphasizes the value of the adrenaline test in cases of leucopenia. If the injection of adrenaline does not produce a leucocytosis he regards this as evidence of cerebral inhibition, and treatment is then directed to restoring to normal the condition of the central nervous system.

[No results of differential blood counts are given, so that the findings described are inapplicable to the leucopenia associated with agranulocytosis, aplastic anaemia, and other conditions.] *L. Firman-Edwards*

1210. **Local Effect of Staphylococcal Toxin. Studies on Blood Vessels with Particular Reference to Phenomenon of Dermonecrosis**

A. THAL and W. EGNER. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **57**, 392–404, May, 1954. 4 figs., 15 refs.

After intradermal injection (into rabbits) of 0·2 ml. of 1 in 10 dilution of staphylococcal toxin an area of necrosis forms which is separated from the surrounding normal tissue by a zone of acute inflammatory infiltration. In due course an eschar forms, and ultimately the necrotic tissue sloughs away from the underlying inflamed tissue.

In order to determine the mechanism of this dermonecrotic effect a number of experiments were carried out at the University of Minnesota Medical School. Toxin was injected into the areolar tissue of the rabbit mesentery between an artery and a vein, and the area observed under a dissecting microscope. Spasm of these vessels was observed which lasted 4 hours or longer. The effect of toxin on capillaries was then tested by applying tiny sponges soaked in toxin directly to the vessel; this caused stasis, probably as a result of altered membrane permeability and haemoconcentration, but no change in the calibre of the vessel.

These experiments indicated that dermal necrosis was the result of prolonged ischaemia. To prove this, an intravenous injection of trypan blue was given to rabbits at various intervals after intradermal injection of toxin. No dye circulated in the area into which toxin was injected except during an initial period of 10 to 20 minutes, when a state of local increased capillary permeability existed. No comparable area of dye exclusion could be demonstrated in control animals in which saline solution was used instead of toxin, or in which heat-inactivated toxin was employed. Administration of heparin did not affect the nature of the dermonecrotic

reaction. Further experiments showed that injection of antitoxin within 10 minutes of toxin injection prevented the development of necrosis; given within 4 hours it minimized the amount of damage, but thereafter it had little effect. *R. B. Lucas*

1211. **Observations on Experimental Anthrax: Demonstration of a Specific Lethal Factor produced *in vivo* by *Bacillus anthracis***
H. SMITH and J. KEPPIE. *Nature* [*Nature* (*Lond.*)] **173**, 869–870, May 8, 1954. 1 fig., 11 refs.

At the Microbiological Research Station, Porton, Wiltshire, the authors have investigated the enigma that in cases of death from anthrax infection no endo- or exo-toxin has been found in cultures of the organism. In guinea-pigs experimentally infected with *Bacillus anthracis* there was a marked bacteriaemia in the 12 hours preceding death. The administration of streptomycin prevented death, provided that it was given before the organisms in the blood exceeded 3×10^6 chains per ml. If the degree of bacteriaemia had progressed further, death regularly occurred in spite of the elimination of all bacteria by streptomycin. Thus bacteriaemia is an essential factor in producing death, but the fate of the animal is already determined at the time when the invasion of the blood stream has reached only 1/300th of its maximum.

Observations suggested that the guinea-pigs died of "shock". When filtered plasma from animals dying of anthrax was injected intradermally into other guinea-pigs, even in a dilution of 1 in 25, extensive areas of oedema were produced. The filtered plasma also killed mice and guinea-pigs when injected intravenously, the signs and symptoms produced resembling those of anthrax. The toxic effect of the infected plasma was completely neutralized by anthrax antiserum. In animals infected with *B. anthracis* the amount of the tissue-damaging factor increased proportionately with the number of bacilli in the blood. Examination of the dying animals showed a raised haematocrit value and total blood nitrogen level, a lowered plasma protein level, anuria, delayed clotting of the blood, subnormal temperature, and histological evidence of acute nephrosis. The authors postulate the presence in the plasma of animals dying of anthrax of a factor which is both lethal and specific. *D. G. ff. Edward*

1212. **Anaerobic Infection in Animals in a State of Sleep.** (Анаэробная инфекция у животных, находящихся в состоянии спячки)
M. R. NECHAEVSKAYA and M. D. PETRENKO. *Журнал Микробиологии, Эпидемиологии ц Иммунобиологии* [*Zh. Mikrobiol.*] 9–11, No. 5, May, 1954.

A condition of hibernation was induced in ground squirrels (*Citellus citellus*) for 2 to 5 days by keeping the animals at an environmental temperature of 6° to 8° C. The animals were then infected with 1 M.L.D. of a culture of *Clostridium welchii*, Strain SR-12, previously established under normal conditions. The infecting dose was always washed to free it from toxins and enzymes and was then injected intramuscularly as a suspension in 0·1 ml. of 25% calcium chloride solution. This type of ground squirrel had not been used for work with *Cl. welchii* before, but in preliminary experiments at normal temperatures the animals proved to be almost as susceptible to infection as guinea-pigs, dying with symptoms of gas gangrene within 18 to 24 hours of infection.

In one group of 8 animals the state of hibernation was terminated 2 days after infection, and in a second group of 6 animals hibernation was terminated 5 days after infection, while a control group of 3 animals were similarly infected but kept at room temperature throughout.

After 48 hours 8 of the 14 animals in the first two groups had developed infiltrations with a small area of necrosis. One animal in the first group died on the 6th day, 3 days after restoration to a normal temperature, and 2 animals in the second group died during hibernation on the 5th day. All the control animals died 18 to 20 hours after infection. Of the surviving animals, 3 were killed on the 7th and 4 on the 12th day after infection. *Cl. welchii* was isolated from the site of infection in all 3 animals which died of the infection during or after hibernation, in all those killed on the 7th day, and in one killed on the 12th day, but in none of these animals was the organism isolated from the internal organs or the blood. Hence it is concluded that in none of the 14 animals infected in a state of hibernation had bacteriaemia occurred.

[These findings are most interesting from a biological point of view, but unfortunately the authors jump to the conclusion that resistance to infection with *Cl. welchii* is increased during a state of depression of the central nervous system—which is not necessarily identical with a state of hibernation.] *K. S. Zinnemann*

CHEMICAL PATHOLOGY

1213. **The Differential Diagnosis between Hepatitis and Obstructive Jaundice.** (Zur Differentialdiagnose: Hepatitis und Verschlussikterus)
G. LAUDAHN. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **79**, 948–952, June 11, 1954. 6 figs., 33 refs.

Of the great number of liver function tests used to differentiate between obstructive and non-obstructive jaundice, the author has found only the thymol turbidity test and measurement of the serum alkaline-phosphatase activity to be reliable. According to Butzengeiger and Lange (*Dtsch. Arch. klin. Med.*, 1952, **199**, 633) the serum iron level is reduced and that of copper greatly increased in obstructive jaundice, whereas in hepatitis the former is much increased and the latter normal or only slightly raised. They therefore suggest that the two types of jaundice may be differentiated by determining the ratio between these two values (the Fe/Cu quotient), which is normally 0·8 to 1·0, but in obstructive jaundice is reduced (0·1 to 0·5) and in hepatitis is increased (1·5 to 3·0).

The author has performed this test at the Wilmersdorf Municipal Hospital, Berlin, on 38 patients with jaundice,

20 of whom had acute hepatitis, 11 biliary obstruction, 5 cirrhosis of the liver, one subacute necrosis, and one cirrhosis and haemolytic anaemia. The normal serum iron level was taken to be 80 to 130 μg. per 100 ml., and the normal serum copper level 90 to 140 μg. per 100 ml. The serum iron concentration was at the lower limit of normal in the 11 cases of obstructive jaundice and that of copper always considerably raised (about 200 μg. per 100 ml.), while the mean Fe/Cu quotient was 0·32, the lowest figure obtained being 0·1; there was good correlation between the reduction in the quotient and the rise in serum alkaline-phosphatase concentration in these cases. In the 20 cases of acute hepatitis there was a characteristic rise in the serum iron level to 190 to 200 μg. per 100 ml. (maximum 360 μg. per ml.), but in most cases the serum copper level was also increased, though to a lesser degree (average 150 to 160 μg. per 100 ml.) so that the Fe/Cu quotient was always above 1·0, the mean value being 1·69, and the maximum 5·53. No such consistent change could be found in the cases of cirrhosis studied, however, though there was a tendency for the serum iron levels to be in the higher range of normal and that of copper to be in the lower range. The value of this test would seem therefore to lie in the help it may give in arriving at a differential diagnosis between obstructive jaundice and hepatitis, the findings in which differ so markedly that the present author considers this to be by far the best method of distinguishing between them.

[It would be of interest to know what results were obtained during the obstructive phase of hepatitis, which is the stage at which the diagnosis and treatment are so particularly difficult to determine.] *H. Lehmann*

1214. **New Liver-function Test**
K. Closs. *Lancet* [*Lancet*] **1**, 910–912, May 1, 1954.

Writing from the Aker Hospital, Oslo, the author describes a new flocculation test of liver function using chloranilic acid (2:5-dihydroxy-3:6-dichloroquinone) as the protein precipitant. The reagent is composed as follows: 0·1% (w/v) chloranilic acid solution 70 parts, 0·85% (w/v) sodium chloride solution 5 parts, glacial acetic acid 0·2 parts, and distilled water to 100. To 2 ml. of the reagent 0·1 ml. of serum is added and mixed well. Readings may be made after 30 minutes by centrifuging or the samples may be left overnight to sediment. The following grading was used:

Precipitate	Supernatant Fluid	Grading
Heavy	Clear	−
Heavy	Opalescent	(−)
Less heavy	Turbid	(+)
Small	Very turbid	+
Trace	Very turbid	++
None	Translucent	+++

The reagent differed from other flocculation tests in that it gave heavy precipitates with normal serum, while with serum from cases of parenchymatous liver disease the amount of precipitate decreased with increasing severity of the liver damage. This phenomenon was greatly influenced by the *p*H, a small increase in the *p*H of the reagent causing all the positive test results to become negative, whereas a decrease in the *p*H had the opposite effect.

The results of this test were compared with those obtained with the Takata–Ara test on 650 blood samples; dissimilar results with the two tests were obtained in 37 instances. The author concludes that the chloranilic acid and Takata–Ara tests seem to be related, in that they both reveal grosser changes in serum protein levels and may be regarded as approximate measures of the severity of liver damage.

[The addition of a new reagent to the already extensive battery of flocculation tests is justified if the test shows advantages in either greater speed or in greater correlation with the degree of liver damage. However, it appears that no two flocculation tests give absolutely identical information and there is a definite advantage in performing at least two flocculation tests with different clinical associations. More information is necessary about the chloranilic acid test, particularly in comparison with other tests such as the thymol and zinc sulphate turbidity tests, rather than with the now rarely used Takata–Ara test.] *M. J. H. Smith*

1215. **The *p*-Aminohippuric Acid Test of Renal Function in Children.** (Der Test mit *p*-Aminohippursäure als Nierenfunktionsprobe beim Kind)
F. H. Dost and T. Goetze. *Monatsschrift fur Kinderheilkunde* [*Mschr. Kinderheilk.*] **102**, 219–223, April, 1954. 2 figs., 27 refs.

Following a single intravenous injection of *p*-aminohippuric acid, the blood aminohippurate level falls exponentially with time. The time–concentration curve can be characterized by the half-life period, that is, the time taken to fall to half concentration from any starting point. This value can be determined either directly from the straight line obtained by plotting log concentration against time, or from the formula

$$t=\frac{(t_2-t_1)\log 2}{\log y_1-\log y_2}$$

where y_1 and y_2 represent the concentrations at times t_1 and t_2. It measures renal clearance in terms of time, and is technically easier to determine than clearance by the conventional method as it does not involve collection of urine.

To perform the test, 35 to 50 mg. of sodium *p*-aminohippurate per kg. body weight is injected intravenously as a 20% solution after an overnight fast (in infants 1 to 2 hours after the early morning feed). Blood samples are taken before the injection and 30, 45, 60, and 75 minutes after it and the blood *p*-aminohippurate level determined. The 30-minute concentration should lie between 0·02 and 0·06 mg. per ml. and should not exceed 0·08 mg. per ml., as blood levels higher than this result in depression of the clearance. Where marked oedema occurs it may be necessary to inject 60 or 70 mg. of hippurate per kg. body weight. No correction for body weight is required.

In tests carried out at the Charité Hospital, Berlin, the following results were obtained. In 5 healthy infants under 3 months of age and weighing about 11 lb. (5 kg.), the half-life period was 22·72±8·5 minutes (range 16·74 to 29·75 minutes); in 5 older infants weighing about 25 lb. (11·3 kg.) it was 17·82±4·53 minutes (range 12·8 to 21·07 minutes); and in 5 healthy schoolchildren weighing about 60 lb. (27 kg.) it was 17·89±8·43 minutes (range 10·9 to 23·64 minutes). The values for ages greater than 3 months were similar to those reported by other workers for adults. For all ages over 3 months the upper limit of normal can be taken as 30 minutes. Raised values were found in patients with primary and secondary nephrosclerosis, chronic nephritis, and renal tuberculosis, but normal values were found in cases of true lipoid nephrosis, unilateral renal disease, and after recovery from acute glomerulonephritis.

M. Lubran

HAEMATOLOGY

1216. **The Use of Substances Depressing Antithrombin Activity in the Assay of Prothrombin**

P. FANTL. *Biochemical Journal* [*Biochem. J.*] **57**, 416–421, 1954. 5 figs., 20 refs.

In this study, carried out at the Alfred Hospital, Melbourne, the ability of various phenols to stabilize thrombin in the presence of the antithrombin of human serum was tested by observing the effect of the buffered phenol on human serum when mixed with a thrombin preparation, the amount of thrombin remaining at measured intervals being determined. It was found that several phenols depressed the antithrombin activity, and one in particular, pyrocatechol, had a marked effect, proving a better depressor than gum acacia. Pyrocatechol was also shown to accelerate the thrombin–fibrinogen reaction.

The author then describes a two-stage method of prothrombin assay in which pyrocatechol is used as a stabilizer of thrombin, and human plasma, made prothrombin-free by treatment with barium sulphate, as the source of the clot. The results of a number of assays of normal mammalian plasma, including human plasma, are given. It seems likely that pyrocatechol acts by affecting the surface structure of fibrinogen, thus making it more sensitive to the action of thrombin.

Marjorie Le Vay

1217. **Purification of Plasma Thromboplastin Factor B (Plasma Thromboplastin Component) and its Identification as a Beta$_2$ Globulin**

P. M. AGGELER, T. H. SPAET, and B. E. EMERY. *Science* [*Science*] **119**, 806–807, June 4, 1954. 1 fig., 11 refs.

It is known that two factors are necessary for the production of thromboplastin in plasma, the antihaemophilic factor and the plasma thromboplastin component (P.T.C.), the latter being also called the Christmas factor or the antihaemophilic factor B. It has recently been proposed to give the antihaemophilic factor the name plasma thromboplastin factor A (P.T.F.-A) and to replace the term P.T.C. by P.T.F.-B. Previous work has shown that P.T.F.-B is present in the β-globulin fraction of the serum. In this paper from the University of California, the authors describe the preparation of a P.T.F.-B concentrate using the β-globulin fraction as starting material. This preparation was compared with normal serum by paper electrophoresis, the filter strips being marked off in transverse divisions. Each segment was eluted and tested for its P.T.F.-B activity. The authors calculate that the concentration of P.T.F.-B in normal plasma must be of the order of 1 mg. or less per 100 ml.

H. Lehmann

1218. **The Erythrocyte Sedimentation Rate in Haemoconcentration Associated with Acute Myocardial Infarction**

B. W. VOLK and S. LOSNER. *American Heart Journal* [*Amer. Heart J.*] **47**, 658–663, May, 1954. 2 figs., 12 refs.

The authors, working at the Jewish Sanitarium, Brooklyn, New York, seek to show that in the presence of haemoconcentration the erythrocyte sedimentation rate (E.S.R.) may not be raised, in spite of marked inflammatory manifestations. Haemoconcentration can occur in massive myocardial infarction, and although there are signs of inflammatory reaction, including fever, leucocytosis, and a raised plasma fibrinogen level, the E.S.R. in some cases may remain initially normal for a long time. Serial studies on 6 patients with massive myocardial infarction showed that the E.S.R. remained normal until the haematocrit value fell below 48. In these cases the increase in the plasma fibrinogen level paralleled the severity of the disease.

Experiments were performed on samples of venous blood from groups of patients with other diseases and varying plasma fibrinogen levels and E.S.R., an increasing haematocrit value being produced by successive removal of plasma. In these experiments the initially elevated E.S.R. was found to return to normal as the haematocrit reading was increased. However, owing to considerable individual deviations, it was impossible mathematically to deduce the E.S.R. at a normal haematocrit value from a given E.S.R. associated with a high haematocrit reading.

E. G. Rees

MORBID ANATOMY AND CYTOLOGY

1219. **Pigmented Nevi, Juvenile Melanomas, and Malignant Melanomas in Children**

H. E. MCWHORTER and L. B. WOOLNER. *Cancer* [*Cancer* (*N.Y.*)] **7**, 564–585, May, 1954. 44 figs., bibliography.

This work, prompted by the work of Spitz in clearly separating the "juvenile melanomata" from the adult malignant melanomata, is based on the histological appearances in 172 pigmented tumours of the skin observed at the Mayo Clinic between 1907 and 1949 in children of 12 years of age or less. Of these, 149 were pigmented naevi (4 junctional, 138 compound, and 7 intradermal), 7 were blue naevi, 11 juvenile melanomata,

and 5 malignant melanomata. The diagnosis of malignancy is often erroneously made in cases of pigmented mole and, in particular, of the clinically benign juvenile melanoma. The latter is situated mainly in the dermis, its cells being either polygonal or spindle-shaped and much larger than the cells of the pigmented mole. The nucleoli are conspicuous, giant cells and mitoses may be seen, and extension into the subcutaneous tissue occasionally occurs. Malignant melanoma may be distinguished histologically by the pleomorphism of the cells, the irregularity and hyperchromasia of the nuclei, and particularly by the occurrence of atypical mitoses. A review of the literature confirms the authors' own conclusion that malignant melanomata of the skin do occur in childhood, but may be regarded as rarities.

H. S. Baar

1220. **Ultra-violet Microscopy of Living Malignant Cells. I. The Interphase Nucleus**

R. J. LUDFORD and J. SMILES. *Journal of the Royal Microscopical Society* [*J. roy. micr. Soc.*] **73**, 173–178, Dec., 1953. 16 figs., 10 refs.

The authors, continuing their study of living cells by means of ultraviolet microscopy, have directed their attention to the constituents of the interphase nucleus. The material examined was derived from transplantable mouse sarcomata and mammary carcinomata, and the cells were flattened between slide and coverslip. Interpretation of the appearances [in photomicrographs of an excellence which we have learned to expect from these workers] leads to the following conclusions.

(1) The nucleolus contains two types of material: nucleolar chromatin and "plasmosomin". Only the former is Feulgen-positive, and it is more absorbent than the latter of light of wave-lengths between 2,570 and 2,750 Å. (2) The interphase chromosomes are represented by fine hyaline filaments bearing chromatin granules, adherent to the inner surface of the nuclear membrane. They appear in ultraviolet photomicrographs as a reticular pattern on this membrane. (3) The nuclear membrane varies in thickness, perhaps with functional activity of the cell. In damaged cells it is much thickened.

M. H. Salaman

1221. **Malignant Cells in Cerebrospinal Fluid**

A. I. SPRIGGS. *Journal of Clinical Pathology* [*J. clin. Path.*] **7**, 122–130, May, 1954. 7 figs., 49 refs.

The examination of stained films of the cerebrospinal fluid (C.S.F.) for tumour cells in cases in which the cause of cerebrospinal pleocytosis is doubtful has been neglected in routine laboratory practice, mainly owing to the difficulting of making satisfactory stained films; indeed, the finding of malignant cells in the C.S.F. has been reported in only 66 cases in the literature, and these are tabulated and briefly discussed. The author, working at the Radcliffe Infirmary, Oxford, then describes 7 cases in which abnormal cells first observed in the C.S.F. in the counting chamber were, in subsequent stained films, identified as tumour cells. In 6 of these cases post-mortem proof was obtained of meningeal dissemination of a malignant growth (2 cases of primary cerebral tumour, 2 of adenocarcinoma, one of reticulosarcoma, and one of myeloma); necropsy was refused in the seventh case.

To make the stained films, as much spinal fluid as can be spared is centrifuged and, after discarding the supernatant, the tube is inverted so that no fluid runs back on to the cells. The cellular deposit is then removed with a platinum loop and smeared on a slide. It is emphasized that the smear must dry instantaneously, and no part of it should be scratched with the loop after it is dry. After being fixed in methyl alcohol for 3 minutes the air-dried films are stained with Leishman's or May–Grünwald–Giemsa stain. If erythrocytes are numerous after centrifuging the C.S.F., one drop of fresh cell-free compatible serum is added to the deposit and a film made exactly as for blood. The method gives excellent results when sufficient cellular deposit can be obtained, but when cells in the C.S.F. are very scanty it cannot be used.

The author concludes that if the examiner is thoroughly familiar with all types of non-malignant cells studied by the same technique, examination of stained films of the C.S.F. for tumour cells is a simple, rapid, and valuable diagnostic procedure and one to be recommended in all doubtful cases of cerebrospinal pleocytosis.

A. Ackroyd

1222. **Examination of Body Fluids for Tumor Cells**

F. VELLIOS and J. GRIFFIN. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **24**, 676–681, June, 1954. 12 figs., 18 refs.

1223. **Primary Tumors of the Heart in Infancy and Early Childhood**

N. H. BIGELOW, S. KLINGER, and A. W. WRIGHT. *Cancer* [*Cancer* (*N.Y.*)] **7**, 549–563, May, 1954. 12 figs., bibliography.

The authors review the primary tumours which occur in the infantile heart and report their findings in 2 cases examined at necropsy at Albany Hospital, New York. In general, primary tumours of the heart occur more frequently in infants and young children than at later ages. The myxomata form an exception to this rule, being found in all age groups with equal frequency, though they must be differentiated from myxoma-like organized thrombi, which are more common in adults. Cushion-like swellings of the valves are not uncommon in infancy; these, which were described on the aortic valves by Lambl in 1856 and are often referred to as Lambl's excrescences, resemble myxomata in structure, but they are tissue malformations and not true neoplasms; the same is true of the so-called valvular haematomata, valvular angiomata, or blood cysts of the valves. Apart from such malformations cardiac lipomata, haemangiomata, and cysts lined with mesothelium have been reported as occurring in early infancy. Of 5 reported cases of intrapericardial teratoma collected by Willis (*J. Path. Bact.*, 1946, **58**, 284), 3 were in infants.

The two cases here reported are examples of two types of primary growth of the heart which are often indiscriminately called rhabdomyomata, only one of which, however, should be regarded as a true neoplasm. The occurrence of striated muscle fibres as an integral part

of this tumour is stressed, and the name " primitive fibroma " is suggested. In the other type the tumour, which in a very high proportion of cases is present at birth, consists of greatly enlarged and vacuolated cardiac muscle fibres [the structure of which, as seen in the photomicrographs reproduced, resembles that of normal Purkinje fibres and justifies a suggestion made recently by Crome (*J. clin. Path.*, 1954, **7**, 137) that these tumours be called " purkinjeomata "]. The lesion occurs frequently in association with tuberous sclerosis. In addition to the nests of Purkinje fibres found in the authors' case, there were also small groups of cells, and even individual cells, which were extremely hydropic and showed cross-striation in parts. This condition is regarded as a " congenital rhabdomyomatosis ", and not as a true neoplastic disease. Its relationship to glycogen-storage disease is discussed.

Finally, the authors deal with malignant cardiac tumours in infancy. Of the few cases reported, only one (a case of malignant teratoma) was found to be completely acceptable, and one (of fibrosarcoma) possibly acceptable. *H. S. Baar*

1224. **Metastasis of Cancer to Cancer**
S. M. RABSON, P. L. STIER, J. C. BAUMGARTNER, and D. ROSENBAUM. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **24**, 572–579, May, 1954. 5 figs., 15 refs.

Five examples of metastasis of cancer to cancer are reported. Adenocarcinoma, primary in the cecum, was found in lymphosarcomatous areas of lung, liver, pancreas and abdominal lymph nodes. Two instances are included of pulmonary carcinoma spreading to clear-cell carcinoma of the kidney. In 2 others, adenocarcinoma of the prostate also invaded renal clear-cell cancer. No conclusion was reached concerning the cause of the rarity of instances of metastasis of cancer to cancer. Antagonism of one new growth to another and a low rate of probability of the meeting of 2 neoplasms in the same portion of an organ were considered.—[Authors' summary.]

1225. **Acinic Cell Adenocarcinoma of the Parotid Gland. Report of Twenty-seven Cases**
J. T. GODWIN, F. W. FOOTE, and E. L. FRAZELL. *American Journal of Pathology* [*Amer. J. Path.*] **30**, 465–477, May–June, 1954. 11 figs., 17 refs.

1226. **The Blood Supply of the Thyroid Gland. II. The Nodular Gland**
N. JOHNSON. *Australian and New Zealand Journal of Surgery* [*Aust. N.Z. J. Surg.*] **23**, 241–252, May, 1954. 17 figs., 11 refs.

At the University of Melbourne the changes in the blood supply of the thyroid gland in cases of nodular goitre were studied with the aid of perfusion and injection techniques. It was shown that the hypertrophic nodule develops from a single thyroid lobule, and that its blood supply is derived from the lobular artery until secondary degenerative changes occur in the nodule, when vascular branches from the capsule may be observed. With the development of the nodule there is compression of the surrounding lobules with the formation of a false capsule containing many large lobular and interlobular vessels. Because of irregular growth and hyperplasia in the nodule the normal symmetrical lobular vascular pattern is disturbed, and many dilated sinusoidal channels become visible. These were shown by perfusion experiments to be closely related to the venous drainage of the nodule and, with giant vessel systems occurring in groups throughout the nodule, formed arterio-venous shunts. The vascular pattern in these nodules is still further distorted and modified by the occurrence within them of haemorrhage and necrosis, which in turn are due to changes in the blood supply brought about by physiological extra-nodular shunts or the pathological intra-nodular arterio-venous shunts already described. *J. B. Wilson*

1227. **Anisotropic Crystals in the Human Thyroid Gland**
M. N. RICHTER and K. S. MCCARTHY. *American Journal of Pathology* [*Amer. J. Path.*] **30**, 545–553, May–June, 1954. 6 figs., 12 refs.

The authors review reports in the literature of the presence of anisotropic crystals in the thyroid gland and present their findings in 928 glands removed surgically or post mortem at the New York University–Bellevue Medical Center and the Presbyterian and Babies Hospitals, New York.

The crystals were found in approximately 40% of the glands examined, increasing in incidence from 12% in subjects in the first three decades of life to 60% in subjects over the age of 60; however, they were found in only 5 out of 45 diffusely hyperplastic toxic glands, usually in areas of involution. Although nearly invisible on ordinary microscopy, they are clearly seen in polarized light. They are polyhedral, spindle-shaped, or irregular, soluble in dilute acids, and insoluble in water and organic solvents.

X-ray diffraction studies of the isolated crystals showed them to consist of calcium oxalate monohydrate. Their significance is unknown. *M. C. Berenbaum*

1228. **Changes in the Lung following Bronchography with Contrast Media Containing Carboxymethylcellulose.** (Die Lungenveränderungen nach Bronchographie mit carboxymethylcellulosehaltigen Kontrastmitteln)
R. HESS. *Thoraxchirurgie* [*Thoraxchirurgie*] **1**, 499–510, April, 1954. 10 figs., 17 refs.

The author has examined, at the Institute of Pathological Anatomy, University of Basle, biopsy specimens or the entire lungs post mortem of 19 persons who had, at various times ranging from 4 days to 4 years before biopsy of the lung or death, received intratracheal injections of 50% " ioduron B " (the diethanolamine salt of diiodopyridone-N-acetic acid) containing 2·5% of carboxymethylcellulose (cellulose–glycollic acid ether) as a viscosity agent for *x*-ray examination.

He found that 4 to 5 days after injection carboxymethylcellulose (CMC) was present in the small bronchi and alveoli of the well-aerated parts of the lung. In the alveoli, which were mostly filled, the substance was sur-

rounded by large, swollen alveolar cells; no giant cells were seen. The alveolar septa were also swollen, as well as being hyperaemic and infiltrated with round cells. In the bronchi CMC was mixed with inflammatory cells and mucus. From the 7th to the 25th day after injection the bronchioles and alveoli contained CMC surrounded by multinucleate giant cells. Alveolar cells containing CMC occurred in the alveoli and in the thickened septa, which underwent progressive fibrosis. In lung samples examined after longer periods the granulation tissue showed a steady increase in fibrosis and a reduction in its cell content; CMC could be demonstrated in the lung up to 266 days after injection.

The author concludes that carboxymethylcellulose is far from harmless, and that its use should be very strictly controlled. *C. L. Oakley*

1229. **The Structural Features of Epiloia, with Special Reference to Endocardial Fibroelastosis**
L. CROME. *Journal of Clinical Pathology* [*J. clin. Path.*] 7, 137–140, May, 1954. 4 figs., 3 refs.

From his study of material from various sources, including 4 personal cases seen at the Fountain Hospital, London, the author enumerates the structural abnormalities which are encountered in epiloia (sclerosis tuberosa) and adds another, namely, fibroelastosis of the heart, which was observed in 2 of his own cases and has been reported in another 2 in the literature.

The commonest lesion in epiloia is tuberous sclerosis of the brain, in which hard nodules are seen in sections stained by the Nissl method as areas of absent or deficient cortical staining, and also in sections stained by any glial method as areas of dense fibrous gliosis situated mainly in the cortex with subependymal nodules ("candle-guttering") projecting into the ventricles; other common lesions are adenoma sebaceum, an acneiform, papular, colourless or brownish rash on the face, purkinjeoma (rhabdomyoma) of the heart, renal tumours, and phakoma of the retina. Although fibroelastosis of the heart has been seen in association with a number of other conditions, its association with epiloia has not received any attention, and its incidence may prove to be significant if it is looked for in future studies. *A. Ackroyd*

1230. **The Pathology of Gastric Arteries, with Special Reference to Fatal Haemorrhage from Peptic Ulcer**
G. R. OSBORN. *British Journal of Surgery* [*Brit. J. Surg.*] 41, 585–594, May, 1954. 19 figs., 9 refs.

Partial gastrectomy was performed on 327 patients at the Derbyshire Royal Infirmary during 1951, and from an examination of the material removed at operation the author attempts to prove that arteriosclerosis of gastric arteries does not occur and is certainly not the cause of haematemesis in patients with gastric ulcer or carcinoma. He states that arterial lesions are commonly found in the region of peptic ulceration, and that they take the form of acute, subacute, or chronic erosion, acute erosion being the typical lesion in fatal cases of haemorrhage from peptic ulcer.

On these findings the author bases his recommendations for treatment, which include immediate blood transfusion and blind gastrectomy. [The clinician may consider that this treatment is too radical, but the paper should be read in the original and the author's plan of treatment thoroughly tested in surgical practice before the soundness of his advice is judged.]

L. Michaelis

1231. **The Stomach in Pernicious Anemia: a Cytologic Study**
B. W. MASSEY and C. E. RUBIN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 481–492, May, 1954. 18 figs., 31 refs.

The false positive cytological diagnosis of gastric malignancy in a patient treated for pernicious anaemia, the diagnosis being based on the finding in the gastric mucosa of abnormally large cells with heavy nuclear membranes, led the authors, at the University of Chicago, to examine smears of aspirated gastric juice from 21 patients with pernicious anaemia in complete haematological remission. An abrasive balloon was introduced into the stomach, and wet smears prepared from the aspirated gastric juice were fixed in ether–alcohol and stained by a modified Papanicolaou technique. In all the patients a minority of the epithelial cells seen in the smears were abnormal ("P.A. cells"); the nuclei were large, often hyperchromatic, and sometimes folded, and vacuolation of the cytoplasm was often present. In 150 control smears from patients with non-pernicious anaemia, histamine-refractory achlorhydria, or gastric carcinoma no such abnormal cells were seen.

A. Wynn Williams

1232. **The Pathogenesis of Diabetic Glomerulosclerosis**
G. S. ANDERSON. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **67**, 241–245, Jan., 1954. 10 figs., 15 refs.

In an investigation carried out at the University of Durham into the pathogenesis of diabetic glomerulosclerosis the author examined 92 kidneys from diabetic patients, in 28 of which there were characteristic Kimmelstiel–Wilson lesions and in 14 other glomerular changes. Since Kimmelstein and Wilson first described a form of hyaline change in the renal glomeruli of diabetic patients three types of intercapillary glomerulosclerosis have been recognized—nodular, exudative, and diffuse. In the present series the nodular type was the most common and the exudative type less so, while the diffuse type was not found in any of the cases.

Two histological features which have hitherto received little or no attention were observed—namely, globular masses of hyaline substance in Bowman's space, and localized dilatations or aneurysms of the glomerular capillaries. The aneurysms were found in 14 of the 92 cases, though rarely together with the hyaline masses.

The pathogenesis of the various lesions is discussed, and it is concluded that nodular glomerulosclerosis may result from the plugging of glomerular capillaries by a protein coagulum from the blood. The cause of glomerular capillary aneurysms is unknown. It is possible that the hyaline nodules form as a result of rupture of the aneurysms, allowing the escape of hyaline material into Bowman's space. *R. B. Lucas*

1233. **Intermediate Nephron Nephrosis from Snake Poisoning in Man. Histopathologic Study**
M. F. AMORIM and R. F. MELLO. *American Journal of Pathology* [*Amer. J. Path.*] **30**, 479–499, May–June, 1954. 14 figs., 42 refs.

A description is given of 3 cases of death from rattlesnake bite which were studied at the Butantan Institute, São Paulo, Brazil. Death occurred in 3 to 7 days from uraemia in each case. The renal lesions were identical with those found in the so-called crush syndrome (haemoglobinuric or lower nephron nephrosis). After a full discussion of the terms used by different authorities in describing the minute anatomy of the kidney, the authors conclude that this condition would be better called " intermediate nephron nephrosis ".

[Without tubular dissection it is difficult to be certain just where in the nephron any lesions are situated.]

J. B. Enticknap

1234. **A Characterisation of Hyaline Arteriolar Sclerosis by Histochemical Procedures**
P. O'B. MONTGOMERY and E. E. MUIRHEAD. *American Journal of Pathology* [*Amer. J. Path.*] **30**, 521–531, May–June, 1954. 10 figs., 24 refs.

The authors have studied the renal arterioles by histochemical methods in 4 cases of hypertension examined post mortem at the Southwestern Medical School, Dallas, Texas, in an attempt to determine the origin of the hyaline material deposited in them. They conclude from their findings that hyalinized arterioles contain lipids (including acidic lipids and cholesterol), polysaccharide sulphates, potassium, free aldehyde and carbonyl groups, and protein-bound sulphydryl, and that they do not contain mucin, glycogen, ascorbic acid, acid or alkaline phosphatase, or non-specific esterase. The tests giving positive results were also positive in the media of normal arterioles, although usually to a lesser degree. The authors suggest that the hyaline material in arteriolar sclerosis is derived locally from necrotic smooth muscle and is not deposited from the blood stream as maintained by Duguid. [The authors overlook the fact that all the substances shown to occur in hyalinized arterioles also occur in, or could be directly derived from, normal blood. Therefore their results could equally be said to support the theory that hyaline material is of haematogenous origin, and the problem of its pathogenesis is not at all elucidated by this work.] *M. C. Berenbaum*

1235. **A Histochemical Study of the Negri Bodies of Rabies**
J. E. MOULTON. *American Journal of Pathology* [*Amer. J. Path.*] **30**, 533–543, May–June, 1954. 15 figs., 30 refs.

The author, working at the University of Minnesota Medical School, Minneapolis, has performed a comprehensive histochemical analysis of Negri bodies in the brains of rabid skunks and mice. They were examined in routine sections, freeze-dried material, touch-impression preparations, and as isolated bodies. Isolation was carried out by homogenization of fresh infected skunk brain tissue in 0·88 M sucrose solution, followed by centrifugation and washing.

The Negri bodies were found to contain protein (ferrocyanide test), alpha amino-acids (ninhydrin reaction), arginine (Sakaguchi's reaction), and tyrosine (Millon's reaction). The inner, basophil, granules of young Negri bodies contained deoxyribose nucleic acid, as shown by a positive Feulgen reaction which was abolished by deoxyribonuclease. Older bodies were Feulgen-negative. These granules also contained organic iron, giving a positive Prussian-blue reaction when unmasked by nitric acid. Negative results were obtained with tests for ribose nucleic acid, glycogen, polysaccharides, acid mucopolysaccharides, ascorbic acid, neutral fat, phospholipids, cholesterol, calcium, inorganic iron, alkaline phosphatase, dehydrogenase, and cytochrome oxidase.

A pink colour was given with Schiff's reagent, with or without previous oxidation with periodic acid, but the author considered this result to be inconclusive. [The possibility of this being due to free aldehydes or acetal phosphatides is not considered.]

M. C. Berenbaum

1236. **A Histological and Histochemical Study of the Neuromuscular Junction in Congenital Amyotonias.** (Étude histologique et histochimique de la jonction neuromusculaire dans les amyotonies congénitales)
C. COËRS. *Acta neurologica et psychiatrica Belgica* [*Acta neurol. Psychiat. belg.*] **54**, 69–77, Jan., 1954. 9 figs., 14 refs.

Bielschowsky expressed the view that the abnormal motor end-plates and fibres in amyotonia congenita were merely immature, but other neurologists have regarded the abnormalities as being degenerative and secondary to muscular atrophy. The present author has studied, at the University Medical Clinic, Brussels, 2 cases of amyotonia congenita and one of Werdnig–Hoffmann's disease (progressive infantile amyotrophy); silver impregnation and vital methylene-blue staining methods were employed for examination of the sections.

He found that in both conditions the muscle spindles, intrafusal muscle fibres, and sensory axons were normal. At necropsy one of the cases of amyotonia congenita showed degeneration of anterior horn cells and poor myelination of the anterior roots, while the muscle fibres were tangled and of various sizes. In both conditions motor nerve fibres were fairly abundant in the muscles, but in amyotonia congenita they tended to end free, between undifferentiated muscle fibres, without making actual contact. In both conditions, also, small but differentiated muscle fibres were supplied by thin motor nerve fibres, sometimes anastomosing, which showed no terminal branching at the end-plate, but sometimes ended in a terminal swelling near a muscle-fibre nucleus. The nerve endings to large muscle fibres were abnormal in that they were unbranched and sometimes had bulbous ends. Cholinesterase activity was diminished at the neuromuscular junction in one of the cases of amyotonia congenita which showed some of the features of congenital myopathy. The author concludes, in agreement with Bielschowsky, that the changes found in the neuromuscular junctions in both the conditions investigated are due to retardation of development rather than to degeneration. *J. Foley*

Bacteriology

1237. **Use of a Cation Exchange Resin for Isolation of Influenza Virus**

K. TAKEMOTO. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **85**, 670–672, April, 1954. 7 refs.

It has been demonstrated by several workers that certain viruses may be adsorbed to, and eluted from, ion-exchange resins, and this paper from the U.S. National Microbiological Institute describes the application of this principle to the isolation of influenza virus from throat washings. A preliminary study was made to determine whether an early egg-passage strain of recently isolated influenza virus A could be adsorbed to the cation-exchange resin "nalcite HCR-X12" (50 to 100 mesh) without loss of egg infectivity. Adsorption of the virus appeared to be complete, and recovery from the eluate (10% sodium chloride) was accompanied by not more than a tenfold decrease in egg-infectivity titre. For isolation of the virus from garglings the resin is added to the fluid and held at 4° C. for 2 hours, shaking every 20 minutes. The supernatant is removed, and 10% sodium chloride solution added to the resin and allowed to stand for 2 hours at 4° C. The supernatant (eluate) is then inoculated into eggs under antibiotic cover in the usual manner.

A comparison was made of the rates of recovery of influenza virus from throat washings by egg inoculation with and without the use of resin. Of 33 specimens from individuals from whom the virus had previously been recovered, 17 gave a positive result with resin and 13 without. Of the latter, 2 were negative with the resin, and of the former, 6 were negative by the ordinary method. In a further series of 73 specimens, all of which had proved negative by ordinary methods, the virus was isolated by the resin method from 10, 4 of which proved positive when the ordinary method was repeated.

[It is not stated whether the method is also applicable to influenza virus B or C.] *J. E. M. Whitehead*

BACTERIA

1238. **Cell Division in *Micrococcus pyogenes* var. *aureus***

R. B. WEBB and J. B. CLARK. *Journal of Bacteriology* [*J. Bact.*] **67**, 94–97, Jan., 1954. 21 figs., 13 refs.

At the University of Oklahoma the authors have re-investigated the morphology of the nuclear bodies in cocci, using a modification of the nuclear staining method of Chance. Air-dried impression smears of *Staphylococcus aureus* were stained for 4 to 5 minutes with 1% crystal violet at *p*H 7·5, washed with tap-water, and, if the organisms had been grown on nutrient agar, treated with 1·5% mercuric chloride for 30 to 45 seconds; with organisms grown on glucose agar, 0·5% mercuric chloride was applied for 15 seconds. The smear was then washed again in tap-water and the cytoplasm decolorized by covering with a film of 8% nigrosin at *p*H 3·5.

The findings in preparations stained by this method, which is more gentle than those involving acid hydrolysis or the use of dyes in organic solvents, agreed closely with those reported by previous workers. Mitotic figures were not observed in cells of normal size, but the authors suggest that mitosis does occur, the nuclear changes being obscured by the deeply staining nuclear membrane, which does not disintegrate during the prometaphase. The constant presence in young cultures on nutrient agar of a small number of large cells with a nucleus several times larger than normal is reported, and it is postulated that these are diploid cells, the normal nucleus being haploid. The diploid cells undergo mitotic division and also meiotic division, which is reported to give a large cell containing four normal-sized nuclear bodies and divided by septa into four individual cells, which eventually form four normal haploid cells.

John M. Talbot

1239. **On the Mode of Release of Tetanus Toxin from the Bacterial Cell**

J. L. STONE. *Journal of Bacteriology* [*J. Bact.*] **67**, 110–116, Jan., 1954. 7 refs.

Recent work by Reynaud and by Stone on the source of tetanus toxin has thrown some doubt on the generally accepted view that it is an exotoxin. The series of experiments described in this paper were undertaken at the laboratories of the Massachusetts Department of Public Health in order to investigate further the mechanism of production of free toxin.

It was found that after cultures of *Clostridium tetani* had been washed repeatedly (up to 15 or 20 times) with 1% peptone in normal saline an appreciable amount of free toxin could still be detected in the washings, as measured by their lethal effect on injection into mice. This free toxin could not have been present in the original culture fluid or it would not have been detectable for more than one or two washings; it must therefore have arisen as a result of the presence of the cells, and five possible mechanisms to account for this are listed: (1) the production of toxin from the washing fluid by the action of an enzyme released from the cells; (2) the presence of unsedimented cells in the supernatant fluid after washing; (3) autolysis of cells with release of toxin; (4) adsorption of toxin on the surface of the cells, with subsequent release; and (5) diffusion of toxin through the cell membrane.

By a series of further experiments [for details of which the original paper should be consulted] these possibilities were subjected to a process of elimination, and diffusion through the cell membrane was left as the most probable

source of the toxin. However, autolysis of the cells could not be entirely ruled out as an additional source, and is thought to be responsible for a considerable proportion of the toxin produced during the growth of the organism in a fluid medium. *John M. Talbot*

1240. **A Simple Blood Medium for Determining the Susceptibility of *Mycobacterium tuberculosis* to Isoniazid (*iso*Nicotinic Acid Hydrazide)**
M. S. TARSHIS. *Journal of Bacteriology* [*J. Bact.*] **67**, 117–122, Jan., 1954. 1 fig., 23 refs.

The author, working at the Kennedy Veterans Administration Hospital, Memphis, Tennessee, has compared the suitability of a human blood medium for determining the sensitivity of tubercle bacilli to isoniazid with that of Herrold's egg-yolk agar and the medium devised by the American Trudeau Society (A.T.S. medium). The blood medium consists of blood–agar base (" difco ") 3 g., glycerol (analytical) 1 g., human bank blood (containing citrate and glucose) 15 ml., and distilled water to 100 ml. The blood–agar base is dissolved in the glycerol and water by heating and the solution sterilized by autoclaving at 15 lb. per sq. inch (1·05 kg. per sq. cm.) for 15 minutes, cooled to 45° C., and the blood then added. Each medium was made up in five separate flasks, to four of which isoniazid was added to give final concentrations of 0·2, 1, 5, and 10 μg. per ml. of medium respectively, and dispensed in 3·5-ml. lots.

The 29 strains of *Mycobacterium tuberculosis* employed were recovered from human sputum after concentration with sodium hydroxide or trisodium phosphate, cultured initially on a solid medium, and then subcultured into Dubos's medium, 0·1-ml. amounts of this subculture being used to inoculate the media containing isoniazid. These cultures were incubated at 37° C. for 28 days before being read.

It was found that the results obtained with the three media were much the same, except that growth on the blood and A.T.S. media was on the whole more profuse than that on Herrold's medium, which in one or two cases resulted in a few colonies appearing at a greater concentration of isoniazid when growing on the former media. The blood medium has the advantage over the other two of being very economical and easily prepared. *John M. Talbot*

1241. **An Inquiry into the Etiology of Acute Bronchiolitis of Infants**
S. H. WOOD, G. J. BUDDINGH, and B. F. ABBERGER. *Pediatrics* [*Pediatrics*] **13**, 363–372, April, 1954. 2 figs., 25 refs.

The bacteriology of acute bronchiolitis in infants was investigated at the Charity Hospital of Louisiana, New Orleans, tracheal secretion and nasopharyngeal swabs from 51 children under 2 years of age being examined. The methods employed for isolation and identification of the organisms and the serological technique are described.

From 36 of the cases *Haemophilus influenzae* was recovered, the organisms being of Type A in 26 and of Type B in 6; the strains in the remaining 4 cases were untypable. An increase in specific antibody titre in the sera was demonstrated in 46 cases—in 37 to Type A and in 9 to Type B. Combined bacteriological and serological evidence of infection with Type A was obtained in 26 cases and with Type B in 5. No cold agglutinins were found in the 26 pairs of sera tested. There was no increase in antihaemagglutinating titre to influenza virus A or B in 46 paired sera, but a fourfold increase in titre to influenza virus C was detected in 5 cases.

The authors conclude that *H. influenzae* Types A and B must be considered to play a part in the aetiology of acute bronchiolitis of early infancy. *R. F. Jennison*

1242. **Trypsin Digesting Medium Added with Horse Plasma for the Culture of the Gonococcus**
V. ROIRON-RATNER. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **30**, 101–102, June, 1954. 8 refs.

SEROLOGY AND IMMUNOLOGY

1243. **A Comparison between the Cutaneous Sensitivity Test and a Modified Antiglobulin Test in Investigation of *Brucella* Infection in Abattoir Workers**
W. J. STEVENSON, A. A. FERRIS, and F. A. LEWIS. *American Journal of Hygiene* [*Amer. J. Hyg.*] **59**, 133–139, March, 1954. 6 refs.

It has been shown by Wilson and Merrifield (*Lancet*, 1951, **2**, 913; *Abstracts of World Medicine*, 1952, **11**, 233) and confirmed by the present authors in a previous study that the Coombs (antiglobulin) test is much more sensitive than direct agglutination for the detection of antibodies to *Brucella abortus*. The authors now report, from the Fairfield Hospital, Melbourne, the results of a comparison between skin sensitivity to " brucellergen " and the presence of circulating antibody as demonstrated by a modification of the Coombs technique. In this study 71 abattoir workers were inoculated intradermally with 0·1 ml. of brucellergen, their reactions being read after 48 hours and graded 1 to 5 according to the degree of erythema, induration, and systemic disturbance. Blood samples were taken just before inoculation and again after 28 to 35 days. All specimens were titrated for " complete antibody " by direct agglutination, and for " incomplete antibody " by using rabbit anti-human globulin (Coombs's reagent). The reading of the reactions and the performance of the serological tests were carried out independently, and correlation was not undertaken until all tests were completed.

It was found that there were 40 positive reactors, of whom only 8 had complete antibody at the first test and 16 at the second, while 37 had incomplete antibody at the first test and 39 at the second. Of the 31 subjects who failed to react to brucellergen only 7 showed some incomplete antibody, and of these only one showed a slight rise in titre at the second test. Positive reactors on the other hand showed a consistent and marked rise at the second test, the average increase being 30-fold. The authors conclude that there is a close correlation

between skin sensitivity to brucellergen and the presence of circulating incomplete antibody to *Br. abortus*. Such discrepancies as were observed were confined to borderline cases, that is, those with 1+ skin reaction and those with an incomplete-antibody titre of 1 in 20 or less. Fairly severe systemic reactions occurred in 16 of the 40 positive reactors in the form of rigors, night sweats, muscle pains, and gastric disturbances which lasted 2 or 3 days; in 3 cases these reactions persisted for 3 to 4 weeks.

[It follows as a corollary that for the diagnosis of undulant fever the Coombs technique for demonstration of incomplete antibody is likely to prove superior to the method of direct agglutination, but that brucellergen testing, owing to its unpleasant side-effects, should be employed with caution.] *L. J. M. Laurent*

1244. **A Hemagglutination Test for Plague Antibody with Purified Capsular Antigen of *Pasteurella pestis***
M. LANDY and R. J. TRAPANI. *American Journal of Hygiene* [*Amer. J. Hyg.*] **59**, 150–156, March, 1954. 6 refs.

Normal sheep erythrocytes do not adsorb the pure capsular protein of *Pasteurella pestis* free from carbohydrate, but can do so after preliminary treatment with tannic acid. These sensitized, tannic-acid-treated erythrocytes when tested with antiplague sera are strongly and specifically agglutinated. In a study carried out at the Walter Reed Army Medical Center, Washington, D.C., the serum of rabbits immunized with (*a*) a suspension of *Past. pestis*, and (*b*) capsular antigen, and the serum of 5 patients suffering from pneumonic plague and that of 14 human volunteer subjects immunized with purified capsular antigen, were all tested for (1) haemagglutination of the sensitized sheep erythrocytes, (2) agglutination of suspension of *Past. pestis*, and (3) complement fixation with capsular antigen. High titres of haemagglutination were obtained in every case, and the test proved to be 20 to 50 times more sensitive than either the bacterial agglutination or the complement-fixation test.

The authors describe in detail the purification of the capsular antigen, the method of treating erythrocytes with tannic acid, of sensitizing them with antigen, and of performing and reading the haemagglutination tests.
L. J. M. Laurent

1245. **The Serological Diagnosis of the Central Nervous Manifestations of Mumps without Parotitis.** (Zur Serodiagnose zentralnervöser Mumpsmanifestationen ohne Parotitis)
R. SIEGERT and H. G. HAUSSMANN. *Klinische Wochenschrift* [*Klin. Wschr.*] **32**, 455–460, May 15, 1954. 2 figs., 43 refs.

Antibodies to the V and S antigens of the mumps virus can be detected in the blood serum and cerebrospinal fluid by a complement-fixation test. In 14 cases of mumps with parotitis the blood antibody levels were determined at the Paul Ehrlich Institute and Municipal Institute of Hygiene, Frankfurt-am-Main, over many months. Anti-S antibody appeared first, and in the first 10 days of the infection gave a higher titre than anti-V antibody. By about the third week, however, the titres of the antibodies were equal and not less than 1 in 160; after this period, both titres fell, but anti-V antibody could still be detected after 8 months.

In 8 cases of mumps without parotitis but with central nervous system manifestations (5 with lymphocytic meningitis, 1 with encephalitis, 1 with optic nerve neuritis, and 1 with convulsions) the serum anti-V titre was 1 in 160 or more in the third and later weeks, the anti-S titre, measured in 6 cases, being 1 in 80 or more at this time; both titres were low in the first week. In 3 cases in which the cerebrospinal fluid was also examined anti-S antibody was not detected, but anti-V antibody was detected in 2 of them.

The authors recommend that for the routine diagnosis of mumps without parotitis serum antibody titres should be determined on a sample of blood taken in the acute stage (1st week) and in the convalescent stage (3rd or 4th week). A fourfold increase in anti-V titre, or for single specimens an anti-V titre not less than 1 in 160, is diagnostic of mumps. In recent infections, if only one blood sample is available or the anti-V titre is not significantly raised, an anti-S titre higher than the anti-V titre may also be considered diagnostic of mumps.
M. Lubran

1246. **Serologic Diagnosis with Respect to Histoplasmosis, Coccidioidomycosis, and Blastomycosis and the Problem of Cross Reactions**
C. C. CAMPBELL and G. E. BINKLEY. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **42**, 896–906, Dec., 1953. 2 figs., 15 refs.

In this paper from the Walter Reed Army Medical Center, Washington, D.C., certain specific antibody patterns which appear to be associated with the various forms of histoplasmosis are described and attention is drawn to potential cross reactions among some of the mycotic antigens used and to the occasional failure of serological reactions in proved cases of mycotic infection.

The antigens used, coccidioidin, histoplasmin, and blastomycin, were crude filtrates respectively of cultures of *Coccidioides immitis*, *Histoplasma capsulatum*, and *Blastomyces dermatitidis* grown on liquid synthetic media. In the serological investigation complement-fixation, precipitin, and collodion-particle agglutination tests were employed. A total of 37 patients with histoplasmosis were examined by these methods. In primary, self-limiting pulmonary infections complement-fixation titres rose steeply to a peak at about 6 weeks, thereafter declining steadily. In cases of chronic infection a high complement-fixation titre was maintained for longer periods, but if the infection became generalized the titre found was consistently low. In certain patients, however, the results of the serological tests were always negative even though *Histoplasma capsulatum* was isolated from the sputum.

Cross reactions between the various mycotic antigens and patients' serum are described in detail, and the difficulty that this phenomenon presented in diagnosis is fully discussed. *G. Payling Wright*

Pharmacology

1247. Urinary Excretion of Adrenocortical Steroids by Patients Receiving Salicylates

M. J. H. SMITH, C. H. GRAY, and J. B. LUNNON. *Lancet* [*Lancet*] **1**, 1008–1009, May 15, 1954. 16 refs.

It has been suggested that salicylates act in rheumatic diseases by stimulating the adrenal cortex via the anterior pituitary to produce adrenocortical steroids, which are considered to be the active therapeutic agents. Some of the evidence supporting this hypothesis and some conflicting with it is here cited.

In the present study, carried out at King's College Hospital Medical School, London, the authors investigated the urinary excretion of adrenocortical steroids in 5 patients receiving salicylates, a paper-chromatographic method which allows separate assay of cortisone, 17-hydroxycorticosterone, and tetrahydrocortisone being employed.

The patients investigated included 3 women with rheumatic fever and 1 woman and 1 man with rheumatoid arthritis. All patients received 4-hourly doses of sodium salicylate totalling 150 to 200 gr. (10 to 13 g.) daily, and the excretion of adrenocortical steroids in 24-hour specimens of urine and the plasma salicylate levels were determined.

In no case did salicylate administration affect the urinary adrenocortical steroid excretion, even when, as in one instance, the dosage of salicylate reached a toxic level. Subsequent administration of corticotrophin to 2 of the patients was followed by a large increase in steroid output. It is clear, therefore, that these results do not support the hypothesis that the therapeutic activity of salicylate depends on the intermediary production of corticotrophin. *Nancy Gough*

1248. Salicylates and the Plasma Level of Adrenal Steroids

R. I. S. BAYLISS and A. W. STEINBECK. *Lancet* [*Lancet*] **1**, 1010–1011, May 15, 1954. 2 figs., 16 refs.

This paper from the Postgraduate Medical School of London reports a study of the plasma level of adrenocortical steroids during salicylate therapy which was undertaken as a direct approach to the problem of whether or not salicylates stimulate the pituitary–adrenal system. Observations were made on 11 patients with either rheumatic fever or rheumatoid arthritis. The plasma levels of 17-hydroxycorticosteroids (cortisone and hydrocortisone) were measured by the authors' modification of the method of Nelson and Samuels (*J. clin. Endocr.*, 1952, **12**, 519) and the plasma salicylate level by the method of Brodie *et al.* Seven of the patients received prolonged treatment with salicylates in a dosage of 0·75 to 1·75 g. 4-hourly, and 4 were given a single dose of 3·3 to 5·3 g., which is sufficient to raise the plasma salicylate concentration to 20 mg. or more per 100 ml.

In no case was there any significant effect on the level of circulating adrenocortical steroids. Hence the authors conclude that salicylates in clinical dosage do not stimulate the pituitary–adrenal system. They add that toxic doses of salicylate may increase the blood level of adrenocortical hormones, but this is merely the normal response to any non-specific poison. *Nancy Gough*

1249. "Darstine": Clinical and Experimental Studies of a New Anticholinergic Drug

A. TOIGO, F. A. GATTAS, and M. A. SPELLBERG. *Gastroenterology* [*Gastroenterology*] **26**, 758–764, May, 1954. 1 fig., 4 refs.

In a study of anticholinergic drugs carried out at the Veterans Administration Hospital, Hines, Illinois, a new quaternary ammonium compound, "darstine" (5-methyl-4-phenyl-1-(1-piperidyl)-3-hexanol methobromide), was given to 17 patients suffering from peptic ulcer. It had no effect on the hyperacidity caused by insulin hypoglycaemia. When given intramuscularly in a dose of 25 mg. it caused a fall in gastric acidity in most cases after about 90 minutes; administration of 50 mg. of the drug gave a more prolonged reduction. When given by mouth in doses of 100 to 200 mg. four times daily it was effective in reducing acidity and especially in relieving pain. Undesirable effects were very slight. The authors consider that the drug does not replace other forms of treatment, but that it may be of value in intractable cases which have failed to respond to other therapy. *V. J. Woolley*

1250. Action of Hexamethonium (C_6) on Intestine, Gall Bladder and Urinary Bladder

N. B. DREYER. *Gastroenterology* [*Gastroenterology*] **26**, 765–768, May, 1954. 2 figs., 3 refs.

The author describes experiments carried out at the Women's Medical College of Pennsylvania, Philadelphia, to test the effect of hexamethonium on the intestine, gall-bladder, and urinary bladder. In anaesthetized cats, the abdominal cavity having been widely opened, cannulae were placed in the gall-bladder and urinary bladder, and a tube tied in the distal end of an intestinal loop which was ligated at the proximal end, the loop and tube being filled with oil and connected to an apparatus which recorded movements or contractions. The method is described in some detail.

The intravenous injection of 0·1 mg. of hexamethonium per kg. body weight caused powerful contractions of the intestine, involving both motility and tone, which were abolished by atropine but not affected by section of the extrinsic nerves. It caused contraction of the gall-bladder, which lasted longer than the contraction produced by acetylcholine or histamine and was abolished by atropine. On the other hand hexamethonium caused inhibition of movement and loss of tone in the urinary

bladder. It is suggested that the constipation which sometimes follows the use of hexamethonium is due to excessive tonus of the large intestine, while urinary retention may be the result of loss of tonus of the musculature of the urinary bladder. *V. J. Woolley*

1251. **Urinary Excretion of Polyvidone**
A. W. WILKINSON and I. D. E. STOREY. *Lancet* [*Lancet*] **1**, 1269–1271, June 19, 1954. 1 fig., 6 refs.

1252. **Vitamin K_1 in Anticoagulant Therapy**
M. TOOHEY. *British Medical Journal* [*Brit. med. J.*] **1**, 1020–1022, May 1, 1954. 1 ref.

The use of vitamin K_1 in anticoagulant therapy, especially the minimum effective dose, is discussed in this paper from New End Hospital, London. The drug was given by mouth in a dosage of 5 to 50 mg. on approximately 96 different occasions to 70 patients receiving anticoagulant therapy. Estimation of the blood prothrombin level about 8 hours after the initial dose showed that in 68 of the 70 patients the drug was entirely effective in counteracting the action of both short-acting and long-acting anticoagulants. The author recommends that vitamin K_1 should be given only if haemorrhage has actually occurred or the blood prothrombin level is so low that haemorrhage is likely. He states that the minimum effective dose necessary to antagonize the action of anticoagulants must be assessed for each patient individually, since uncontrolled administration of vitamin K_1 may increase the risk of further thromboembolism. In general, patients receiving the short-acting anticoagulants (phenylindanedione, ethyl biscoumacetate) require small doses (5 to 15 mg.) of the vitamin; those receiving the long-acting anticoagulants (dicoumarol, phenylpropylhydroxycoumarin, *cyclo*cumarol) require 10 to 25 mg.; while in cases of frank haemorrhage in which continued anticoagulant therapy is not intended still larger doses of 25 to 50 mg. may be necessary.

[This paper presents a personal viewpoint. Further work, in which consideration is given to other factors concerned in blood coagulation, is required to support the conclusions reached.] *G. B. West*

1253. **Clinical Evaluation of Toryn, a New Synthetic Cough Depressant**
W. H. ABELMANN, E. A. GAENSLER, and T. L. BADGER. *Diseases of the Chest* [*Dis. Chest*] **25**, 532–541, May, 1954. 2 figs., 5 refs.

The cough depressant effect of the synthetic compound "toryn" (bis-[1-(carbo-B-diethyl-aminoethoxy)-1-phenyl-*cyclo*pentane]-ethane disulphonate) was studied at Boston City Hospital (Harvard Medical School) in 26 out-patients suffering from severe, irritating, chronic cough, patients with a predominantly productive cough being excluded. Four sets of identical tablets were prepared; one was a placebo while the others contained 16·2 mg. of codeine sulphate, 5 mg. of dihydrocodeinone bitartrate, and 10 mg. of toryn respectively, each being given for a week at a time after each meal, physicians, nurses, and patients being unaware of their identity or the order in which they were given. Of the 26 patients, 20 completed the full course of each drug. The results were evaluated by means of a daily report card on which the patient recorded the amount of cough and sputum at the end of each day, and by weekly assessment at an interview with the physician.

A decrease of cough was noted by the patient on 43% of the days on which he took toryn, the corresponding figures being 31% of days with the placebo, 55% with codeine, and 54% with dihydrocodeinone. Analysed statistically, the difference between the figures for the placebo and toryn is probably significant, but this cannot be considered to have been established, whereas in the case of the other two drugs the difference is definitely significant. [On the other hand an increase in cough was noted on 9% of days with the placebo, on 12% with toryn and dihydrocodeinone, and on 22% of the days on which codeine was taken.] In 7 in-patients there was a slight decrease of sputum following the administration of each of the three drugs. Drowsiness and dizziness appeared to be the most prominent side-effects of toryn, especially after larger doses, while nausea was noted occasionally. *Robert Hodgkinson*

1254. **Anticonvulsant Properties of 5:5-Diphenyl-tetrahydroglyoxaline-4-one (SKF No. 2599)**
L. S. GOODMAN, E. A. SWINYARD, W. C. BROWN, and D. O. SCHIFFMAN. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **110**, 403–410, April, 1954. 1 fig., 19 refs.

At the University of Utah College of Medicine, Salt Lake City, the anticonvulsant properties of 5:5-diphenyl-tetrahydroglyoxaline-4-one (" SKF 2599 ") and diphenylhydantoin were assayed quantitatively by a variety of tests in experiments on mice and rats subjected to maximal electric shocks; a limited number of tests were also carried out on cats, albino rabbits, and psychiatric patients. The drugs were administered orally to the animals in a homogenized aqueous suspension containing 10% acacia and assayed at the time of peak effect of the electric shock.

In mice SKF 2599 was found to be less neurotoxic and less potent than diphenylhydantoin in its ability to modify the seizure pattern, but was more potent in elevating the seizure threshold. In rats the two drugs were equipotent in modifying the maximal-shock seizure pattern and in raising the threshold for minimal-shock seizures in hyponatraemic animals. SKF 2599 also raised the minimal electric shock threshold in normal rats, and exhibited marked ability to prevent maximal convulsions induced by electric shock and leptazol in cats and rabbits. SKF 2599 was found to modify or abolish therapeutic electric shock in psychiatric patients, but occasionally produced nausea and drowsiness.

Discussing the chemical structure of this substance the authors conclude that the substitution of two atoms of hydrogen for the oxygen on the carbon in Position 2 of diphenylhydantoin to yield SKF 2599 decreases potency and toxicity, but increases the margin of safety. The oxygen on the carbon of the urea moiety of diphenylhydantoin would appear not to be essential for anticonvulsant activity. *Norval Taylor*

Chemotherapy

1255. **Revival of Tubercle Bacilli after Prolonged *in vitro* Exposure to Isoniazid**

M. W. Fisher. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **85**, 538–540, April, 1954. 9 refs.

Tubercle bacilli of the H37Rv strain, which had grown for 14 days in Dubos's liquid "tween"–albumin medium, were washed and suspended in phosphate buffer (*p*H 6·8) containing 1 mg. of isoniazid per ml. and held at room temperature for 5 weeks. At weekly intervals an aliquot of the cells was taken, centrifuged and washed twice in buffer, and then inoculated into a liquid basal synthetic medium plus 10% bovine serum, and into the same medium plus various substances known to antagonize the action of isoniazid (haemin, potassium ferricyanide, sodium pyruvate, and manganous chloride). The subcultures were incubated at 37° C. for 5 weeks and inspected for growth.

Whereas no tubercle bacilli could be recovered after 2 weeks' exposure to isoniazid by subculture in medium containing serum, it was possible to recover the organisms after 5 weeks' exposure when subculture was made into medium containing potassium ferricyanide, haemin, or sodium pyruvate. The sensitivity to isoniazid of the bacilli so recovered was similar to that of the parent culture.

In further experiments haemin was shown to have the same reversing action when added directly to cultures in basal medium containing isoniazid in concentrations up to 2·5 μg. per ml. If, however, as little as 0·01% of tween 80 was added to the medium in which the cells were exposed to isoniazid, no such reversal of bacteriostatic effect took place. The possible mechanism of the reversal of the bacteriostatic effect of isoniazid is discussed.

J. E. M. Whitehead

1256. **1:6-Di-4′-chlorophenyldiguanidohexane ("Hibitane"). Laboratory Investigation of a New Antibacterial Agent of High Potency**

G. E. Davies, J. Francis, A. R. Martin, F. L. Rose, and G. Swain. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **9**, 192–196, June, 1954. 3 refs.

During an investigation of the biological and antibacterial properties of a number of bisdiguanides it was found that the most active was 1:6-di-4-chlorophenyldiguanidohexane (serial number 10,040; "hibitane"), which displayed bacteriostatic action against a wide range of bacteria *in vitro*, Gram-positive organisms being somewhat more sensitive than Gram-negative ones. The substance had feeble activity against bacterial spores, but in a concentration of 1 in 1,000,000 it inhibited the growth of *Mycobacterium tuberculosis*. Bactericidal activity against *Staphylococcus aureus* was judged by plating out after the addition of egg-yolk, which inhibits the bacteriostatic effect of hibitane; milk, blood serum, and nucleic acid do not interfere with its bacteriostatic action. The bactericidal action of the drug was unusual; in a dilution of 1 in 200,000 it killed 99·9% of the bacteria within 5 minutes, but very much higher concentrations were required to kill 100%, and even in a concentration of 1 in 20,000 it did not kill all the organisms in 10 minutes. The surviving organisms were not, however, apparently naturally resistant to the drug, since the same phenomenon occurred when they were re-grown and retested. Its bactericidal activity was found to increase with increasing *p*H of the medium from 5·25 to 7·97, but was independent of the size of the inoculum. No increase in resistance to hibitane was noted after repeated attempts to produce resistance in several strains of *Staph. aureus* and *Pseudomonas pyocyanea* by serial transfers in a number of different media.

Hibitane was compatible *in vitro* with the common antibiotics and had no effect on the phagocytic activity of human leucocytes in a concentration of 1 in 10,000. The drug was shown to have a low acute toxicity in mice, and when given for a year in a solution of 1 in 2,000 in water to a group of 14 rats and their progeny as their only source of drinking water it produced no detectable ill effects. When hibitane and streptococci were injected together intraperitoneally in mice the drug had only a slight therapeutic effect, and presumably has little action on organisms which survive contact with it and which subsequently invade the body. It was, however, highly efficacious in mice when applied locally as a 1% solution to experimental wounds infected with streptococci. Under the same conditions 1% proflavine had very little effect.

Derek R. Wood

AMOEBICIDES

1257. **The Chemotherapeutic Properties of Win 5047 ("Mantomide"), a New Synthetic Amebacide**

E. W. Dennis and D. A. Berberian. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 554–560, May, 1954. 9 refs.

In a series of tests carried out at a pharmaceutical research laboratory, "Win 5047" (N-(2:4-dichlorobenzyl)-N-(2-hydroxyethyl)dichloroacetamide; "mantomide") was selected for further study from among a number of compounds synthesized in the search for an effective amoebicide which would be non-toxic and relatively inexpensive. The drug is a white crystalline powder with a slightly bitter taste and is relatively insoluble in water.

Assay of its amoebicidal activity *in vitro* was carried out by inoculating serially diluted solutions of Win 5047 in Hansen's egg-infusion medium with sediment from a rich 72-hour culture of *Entamoeba histolytica* and counting microscopically the number of living amoebae in the

sediment of a single-drop sample from each tube at the end of 30 and 48 hours. All amoebae were killed by the drug in a concentration of 1 in 40,000 at the end of 30 hours, and in a concentration of 1 in 80,000 at the end of 48 hours. At these concentrations the associated bacteria grow freely, so that the amoebicidal activity may be presumed to be direct.

Tests *in vivo* were carried out against *E. muris* (*E. criceti*) in naturally infected hamsters weighing 100 to 110 g. which were treated orally twice daily for 4 consecutive days with suspensions of the drug in 10% autoclaved gelatin. On the 5th day the animals were killed and caecal scrapings examined microscopically. The dose found to clear 50% of the animals of infestation was $12{\cdot}4 \pm 3{\cdot}1$ mg. per kg. body weight per day as estimated by a log probit method; 100% clearance was obtained with between 37·5 and 75 mg. per kg. per day. Win 5047 produced no bloating of the caecum or alteration of the caecal flora in the hamsters, although these changes were noted after treatment with corresponding doses of chlortetracycline and oxytetracycline. The drug in doses up to 2 g. per kg. per day did not perceptibly alter the caecal flora. Faecal specimens from 3 monkeys infected with *Entamoeba coli* and treated with 25 mg. per kg. per day for 5 days became negative within 48 hours and were still negative 14 days after the end of treatment.

The acute oral single-dose LD_{50} for mice was greater than 16 g. per kg. body weight. In subacute toxicity tests hamsters given the drug twice daily for 5 days tolerated 2 g. per kg. per day, white rats tolerated single daily doses of 8 g. per kg. per day given for 5 days, and monkeys given 200 mg. per kg. body weight daily for 21 days remained well and at necropsy showed no gross or microscopical changes that could be attributed to the drug. Preliminary absorption and excretion studies showed the drug to be well absorbed from the gastro-intestinal tract.

Three adult human patients infected with *E. histolytica* —one a mild case of chronic amoebiasis, the second a symptomless carrier, and the third with moderately severe symptoms—were successfully treated with daily doses of 0·75 to 1·0 g. for 8 to 10 days. No undesirable side-effects were produced. *I. M. Rollo*

1258. **The Treatment of Amebiasis with Win 5047 (Mantomide). N-(2-4-dichlorobenzyl)-N-(2-hydroxyethyl) dichloracetamide**

E. H. Loughlin and W. G. Mullin. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 570–573, May, 1954. 1 ref.

At the Flower and Fifth Avenue Hospitals, New York, 24 cases of chronic amoebiasis, in which the diagnosis was established by microscopical examination of faeces, were treated with the new amoebicide Win 5047 [see Abstract 1257] and response to treatment assessed by observation thereafter for a minimum period of 6 weeks. This period was chosen in order to reduce the possibility of re-infection obscuring the results, but most of the patients were under observation for longer periods. The dosage, based on age, was 250 mg. 3 times a day for 8 days for patients under 5 years of age, 500 mg. 3 times a day for 10 days for those aged 5 to 10 years, and 750 mg. or 1 g. 3 times a day for 10 and 8 days respectively for those over 10 years.

One patient receiving the 750-mg. dosage did not respond to treatment and the course was repeated for 10 days with doses of 1 g., upon which the faeces became negative for *E. histolytica*, but cysts reappeared in the seventh post-treatment week; the circumstances in this case pointed to failure of the drug, although the possibility of re-infection could not be dismissed. In all the other cases treatment was regarded as satisfactory and no evidence of toxicity or intolerance was noted. In one adult patient tolerance was tested by giving 2·5 g. of the drug twice a day for 5 days; no ill effects were noted and *E. histolytica* did not reappear during the 6-week period of observation. The possibility of using this inexpensive drug for controlling amoebiasis in endemic areas either in therapeutic doses or as a prophylatic (together with improved sanitation) is suggested.

I. M. Rollo

CHEMOTHERAPY OF TUMOURS

1259. **Sarkomycin, an Anti-cancer Substance Produced by *Streptomyces***

H. Umezawa, T. Yamamoto, T. Takeuchi, T. Osato, Y. Okami, S. Yamaoka, T. Okuda, K. Nitta, K. Yagishita, R. Utahara, and S. Umezawa. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 514–520, May, 1954. 1 fig., 11 refs.

Products obtained from 200 soil *Streptomyces* were tested for anti-cancer activity at Keio University, Tokyo, and the University of Tokyo; of these, sarkomycin proved to be the most effective and of low toxicity.

This compound is produced by a strain similar to *S. erythrochromogenes*, and was isolated from the culture medium by extraction with ethyl acetate, evaporation *in vacuo* to a brown syrup, dilution in water, neutralization with sodium bicarbonate, removal of a precipitate formed by addition of saturated potassium alum solution, and final re-extraction with ethyl acetate to yield, on removal of the solvent, a light brown syrup of high potency.

Since the antibacterial and anti-cancer activities ran parallel, sarkomycin was assayed during the progress of its purification by its antibacterial action on *Staphylococcus aureus* 209-p. The free acid and the sodium salt were soluble in water and the lower alcohols, but the molecular structure was not characterized more exactly by a series of chemical tests. It had a bacteriostatic effect on many organisms, which was influenced by the presence of cysteine or serum, and it was more toxic by subcutaneous than by intravenous injection.

The action of sarkomycin on tumour cells was studied, the ascitic and subcutaneous types of Ehrlich's mouse carcinoma being used. At the most effective dosage range (0·5 to 4·0 mg. a day) injected intraperitoneally for 12 successive days, 75% of mice with ascitic tumours survived for more than 35 days (controls 12 to 18 days),

and lesser effects were obtained by intravenous injection or by oral administration.

Mice with subcutaneous tumours received one injection a day for 15 days, and the average weight of the tumours in the treated group was 1·5 g., as against 3·7 g. in the control group. *H. G. Crabtree*

1260 (*a*). **Therapeutic Trials of Actinomycin in Hodgkin's Disease.** (Essais de traitement de la maladie de Hodgkin par l'actinomycine)
—. BERTRAND-FONTAINE, J. MALLARMÉ, J. SCHNEIDER, and J. DEBRAY. *Presse médicale* [*Presse méd.*] **62**, 737–738, May 15, 1954.

1260 (*b*). **Therapeutic Trials of Actinomycin C.** (Essais thérapeutiques concernant l'actinomycine C)
P. CROIZAT. *Presse médicale* [*Presse méd.*] **62**, 738, May 15, 1954.

1260 (*c*). **Preliminary Results of the Therapeutic Use of Actinomycin C.** (Premiers résultats de l'emploi de l'actinomycine C en thérapeutique)
C. GERNEZ-RIEUX and M. GOUDEMAND. *Presse médicale* [*Presse méd.*] **62**, 739–740, May 15, 1954.

1260 (*d*). **Experiments with Actinomycin.** (Expérimentation de l'actinomycine)
R. HUGUENIN, R. TRUHAUT, and J. S. BOURDIN. *Presse médicale* [*Presse méd.*] **62**, 740, May 15, 1954.

1260 (*e*). **Preliminary Results of the Therapeutic Application of Actinomycin C.** (Premiers résultats de l'application de l'actinomycine C en thérapeutique)
M. JANBON. *Presse médicale* [*Presse méd.*] **62**, 741, May 15, 1954.

1260 (*f*). **Preliminary Results of the Treatment of 12 Cases of Hodgkin's Disease with Actinomycin C.** (Premiers résultats de 12 maladies de Hodgkin traités par l'actinomycine C)
R. MARTIN and J. P. MUNIER. *Presse médicale* [*Presse méd.*] **62**, 741–742, May 15, 1954.

1260 (*g*). **Therapeutic Trials of Actinomycin C in Certain Malignant Diseases of the Blood.** (Essais de traitement de certaines hémopathies malignes par l'actinomycine C)
J. OLMER. *Presse médicale* [*Presse méd.*] **62**, 742–743, May 15, 1954.

1260 (*h*). **Preliminary Results of the Treatment of Hodgkin's Disease and Malignant Tumours with Actinomycin C.** (Premiers résultats du traitement de la maladie de Hodgkin et des tumeurs malignes par l'actinomycine C)
A. RAVINA and M. PESTEL. *Presse médicale* [*Presse méd.*] **62**, 743–744, May 15, 1954.

Publicity given in the popular press to German reports that a variety of actinomycin, actinomycin C, was of value in the treatment of certain types of cancer led to a great demand for the drug in France. Only a small supply of actinomycin C being available, this was issued to a few selected centres distributed throughout the country for clinical trial by teams of workers whose preliminary results are now reported.

The first seven reports are all very similar. In all, 118 cases were treated, mostly of Hodgkin's disease and allied disorders, though a few other forms of cancer were included. The drug was given by intravenous injection in doses of 200 or 400 μg. up to a total of 1,000 to 12,000 μg. In a few cases a temporary remission was observed, usually a reduction in the size of superficial lymph nodes, but these remissions were never more than transient and all the observers are agreed that the results were much inferior to those obtained with radiotherapy or nitrogen mustard. From these reports the general conclusion is reached that if actinomycin has any place at all in therapy, it can only be in combination with other measures or in cases which have become resistant to other forms of treatment. Toxic effects included anorexia, nausea, abdominal pain, diarrhoea, stomatitis, jaundice, and alopecia.

The report of Ravina and Pestel from the Hôpital Beaujon, Clichy, is unique in its optimism. Remissions were achieved in all of 4 cases of Hodgkin's disease, and they also obtained good remission in one case each of metastatic carcinoma of the liver, lymphosarcoma, lymphoid follicular reticulosis, and malignant ascites. Failure is recorded in 5 cases of other forms of cancer. The method of treatment used by these authors differed in some respects from that used by the other teams, the drug usually being given by intravenous drip infusion lasting 3 to 4 hours rather than as a single daily injection, while in some cases the daily dose was 800 μg. They also obtained good results by local injections of actinomycin into malignant effusions and achieved a good remission in one case of carcinoma of the bladder treated by intravesical injection.

[It remains possible that actinomycin may be so rapidly excreted that a single intravenous injection daily fails to maintain an adequate concentration in the body. The optimistic German results were obtained with subcutaneous and intramuscular injections, which produce severe local irritation. There appears to be a case for the further trial of this drug by slow intravenous infusion and local application, and it is to be hoped that such a trial, if carried out, will be more carefully planned and controlled.] *P. C. Reynell*

1261. **Observations on the Anticancer Activity of 6-Mercaptopurine**
H. E. SKIPPER, J. R. THOMSON, G. E. ELION, and G. H. HITCHINGS. *Cancer Research* [*Cancer Res.*] **14**, 294–298, May, 1954. 7 refs.

1262. **Negative Effects of Some Metabolite Analogs in Human Neoplasms**
J. L. STEINFELD, L. P. WHITE, N. L. PETRAKIS, and M. B. SHIMKIN. *Cancer Research* [*Cancer Res.*] **14**, 315–318, May, 1954. 1 fig., 14 refs.

Seven chemicals structurally related to vitamins, purines, and amino acids were tested for possible chemotherapeutic effects on 28 patients with advanced neoplastic disease. Under the specific conditions of the procedures and type of patients, no beneficial effects on the patients or objective adverse effects upon the neoplasms were elicited with 8-azaguanine, benzimidazole, flavotin, *iso*riboflavin, aminopterin, *iso*nicotinic acid hydrazide, or ethionine.—[Authors' summary.]

Infectious Diseases

1263. **A Roentgen Study of the Gastrointestinal Tract in Proven Cases of Sarcoidosis with a Review of the Literature**

S. H. LORBER, H. SHAY, and H. WOLOSHIN. *Gastroenterology* [*Gastroenterology*] **26**, 451–461, March, 1954. 5 figs., 37 refs.

To determine whether the gastrointestinal tract is involved in cases of sarcoidosis the authors examined radiologically the oesophagus, stomach, and small intestine of 21 patients at Temple University Hospital, Philadelphia, with proven Boeck's sarcoid. In 17 of these cases, in addition to barium-meal examination, a small-intestinal enema was given, the technique employed being a modification of that described by Gershon-Cohen and Shay (*Amer. J. Roentgenol.*, 1939, **42**, 456). In spite of this careful examination the authors were unable to find any abnormality which could be attributed to sarcoid. A review of the literature revealed that gastrointestinal involvement in sarcoidosis is rare, and the authors give their reasons for doubting the validity of some of the reported cases. *Sydney J. Hinds*

1264. **Infectious Mononucleosis Encephalitis**

F. C. WALSH, C. M. POSER, and S. CARTER. *Pediatrics* [*Pediatrics*] **13**, 536–543, June, 1954. 2 figs., 22 refs.

1265. **Terramycin and Chloramphenicol in the Treatment of Enteric Fever**

B. J. VAKIL, B. B. YODH, M. J. SHAH, and K. U. JHATAKIA. *Indian Journal of Medical Sciences* [*Indian J. med. Sci.*] **8**, 151–156, March, 1954. 15 refs.

The treatment of typhoid fever with chloramphenicol is generally recognized to be satisfactory except in two respects: (1) the occurrence of relapses, and (2) the treatment of carriers. This short study, reported from Nilratan Sircar Medical College, Calcutta, of 12 cases treated with "terramycin" (oxytetracycline) in various doses and 8 cases treated with a combination of oxytetracycline and chloramphenicol was undertaken in the hope of obtaining some improvement in these two respects.

Oxytetracycline alone was found to be unreliable for treatment of the acute stage. As the authors point out, this failure *in vivo* is remarkable in view of the inhibition of *Salmonella typhosa in vitro* by oxytetracycline in a weaker concentration than that of chloramphenicol. The combined therapy was satisfactory, but the response obtained was no better than that to chloramphenicol alone. Chloramphenicol therefore still remains the drug of choice in the treatment of typhoid fever. In this small series there were no major complications and no relapses, and from this point of view the combination of chloramphenicol with oxytetracycline may be worthy of further trial. *H. Stanley Banks*

1266. **The Treatment of Hepatitis with Infusions of Ascorbic Acid.** (Hepatitistherapie mit Ascorbinsäure-infusionen)

H. BAUR and H. STAUB. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **84**, 595–597, May 22, 1954. 2 figs., 21 refs.

The authors report from the University Medical Clinic, Basle, the results of treatment with massive doses of ascorbic acid in 11 cases of infective hepatitis, and compare these results with those obtained in 159 cases treated during the preceding 6 years by complete rest in bed, diet rich in protein and carbohydrate and poor in fat, the parenteral administration of vitamins of the B-complex, and application of hot packs over the liver and abdomen. Additional treatment in 136 cases treated between 1947 and 1950 consisted in the administration of insulin and glucose, various vitamins, aureomycin, and choline and methionine. From 1950 onwards a daily intravenous infusion of 1 litre of physiological saline, with or without the addition of vitamins, was included in the regimen, 59 cases being thus treated. In the present series of 11 cases, 10 g. of ascorbic acid was given daily by intravenous infusion for 5 or 6 days in 1 litre of saline.

Comparison between the different groups was based on the degree and course of the bilirubinaemia, the results of the Takata–Ara reaction, the urinary bilirubin and urobilin excretion, and on the length of stay in hospital. As the authors admit, the assessment of the results was made more difficult by the adoption of different therapeutic regimens and by the fact that over the period of the present survey the case mortality from infective hepatitis fell from 19% in 1946 to 9% in 1947, 7% in 1948, and to 0 to 1% after 1948. They are, however, of the opinion that after 1950 there was no significant change in the natural course of the disease.

The results, which are tabulated, show that, on the average, the 11 patients treated with massive doses of ascorbic acid returned to normal rather more quickly than those in any of the earlier groups. [However, the overlap between all groups is such that the authors' contentions as to the efficacy of this treatment can hardly be accepted.] The possible mode of action of ascorbic acid on the general metabolism or as a virucidal agent is discussed. *H. F. Reichenfeld*

1267. **Hemorrhagic Fever: Study of 300 Cases**

G. M. POWELL. *Medicine* [*Medicine (Baltimore)*] **33**, 97–153, May, 1954. 24 figs., 28 refs.

1268. **Potential Vectors and Reservoirs of Hemorrhagic Fever in Korea**

R. TRAUB, M. HERTIG, W. H. LAWRENCE, and T. T. HARRISS. *American Journal of Hygiene* [*Amer. J. Hyg.*] **59**, 291–305, May, 1954. 5 figs., 13 refs.

Tuberculosis

1269. **The Effect of Antimicrobial Therapy on the Prognosis of Primary Tuberculosis in Children**
E. M. LINCOLN. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 682–689, May, 1954. 1 fig.

The case fatality rate amongst 980 children with primary pulmonary tuberculosis admitted to the Bellevue Hospital, New York, between 1930 and the end of 1946 (that is, before the introduction of streptomycin therapy) was 21·5%. Nine-tenths of the deaths occurred within a year of diagnosis, and 60% were due to meningitis. The only chemotherapy available during this period was with sulphones, introduced in 1944, and this had apparently effected a few cures in cases of miliary tuberculosis, but failed to cure meningitis or other complications. Between 1947 and 1951, when streptomycin and PAS were available in addition to sulphones, 421 cases of primary pulmonary tuberculosis were admitted to the hospital, but only those with meningitis, miliary spread, and locally progressive lesions (35% of the total) were given chemotherapy. The death rate for the whole group fell to 5%, and the mortality from meningitis from 100 to 37%.

In 1952 isoniazid therapy was added to the previous forms of treatment. As a result, in a further group of 129 cases treated during 1952–3 the over-all fatality rate was reduced to 1·5%, and the death rate from meningitis to 12%. Streptomycin was not used in treating many of the uncomplicated, mainly asymptomatic cases, because no investigator has shown that resolution is hastened by this drug, and also because of the dangers of promoting drug resistance or causing damage to the hearing. Meningitis occurred in many children already receiving intensive streptomycin therapy for other reasons, but in no case treated with isoniazid has meningitis developed. If this observation is substantiated by other workers, the author suggests, " it may radically change the present indications for specific therapy " and the treatment of all cases of primary tuberculosis for one year with isoniazid in order to prevent complications, especially meningitis, may have to be considered.

M. Baber

1270. **Comparative Trial of Vaccination against Tuberculosis by Multiple Dermal Puncture with Petragnani's Anatuberculin and B.C.G.** (Prove comparative di vaccinazione antitubercolare per multipuntura dermica, con " anatubercolina integrale Petragnani C." e B.C.G.)
G. BUONOMINI, G. SANTOPADRE, and A. PREVITERA. *Rivista dell'Istituto sieroterapico Italiano* [*Riv. Ist. sieroter. ital.*] **29**, 125–150, March–April, 1954. 7 figs., 34 refs.

The authors describe the results of experiments with B.C.G. and the anatuberculin of Petragnani (prepared from formol-killed bacilli) carried out at the Institute of Hygiene and Microbiology, University of Pisa. The preparations employed are described. The inoculations were carried out by the multiple skin-puncture method on 305 guinea-pigs, which were observed for up to 17 months.

The production of allergic reactions to tuberculin and whole tubercle bacilli was similar in animals vaccinated by both methods. Tuberculin allergy lasted as long in animals vaccinated with anatuberculin as in those inoculated with B.C.G. Koch's phenomenon could be demonstrated 16 months after vaccination with both products. The authors analysed statistically the average weight curves, the monthly mortality, the survival rate, and the morbid anatomical findings in vaccinated animals which had been subjected to a challenge infection. They found no difference between the two vaccines, and urge the wider use of Petragnani's anatuberculin on the grounds that it is more readily standardized.

R. F. Jennison

1271. **Studies on the Diagnostic Value of Modern Serological Tests for Tuberculosis**
H. HONKAPOHJA. *Annales medicinae experimentalis et biologiae Fenniae* [*Ann. Med. exp. Biol. Fenn.*] **32**, Suppl. 3, 1–84, 1954. 10 figs., bibliography.

RESPIRATORY TUBERCULOSIS

1272. **The Role of Perforation of Hilar Lymph Nodes into the Bronchial Tree of Adults**
H. ISELIN and F. SUTER. *Diseases of the Chest* [*Dis. Chest*] **25**, 302–311, March, 1954. 7 figs., 10 refs.

Examination by bronchoscopy of 1,228 patients with pulmonary tuberculosis at Davos-Platz, Switzerland, revealed 38 cases of acute perforation into the large bronchi from tuberculous nodes. In a further 81 cases there was evidence of previous perforation, and it is therefore considered that perforation had occurred in about 10% of this group of patients. The age of the 38 patients varied considerably, but 26 (68%) of them were between 18 and 30 years of age; only 7 were men. Symptoms were not a reliable guide to diagnosis, and in most cases the condition was suspected because of changes in the lung. The perforations varied in size, some being large craters while others were boil-like eruptions.

Perforation, with its associated destruction of epithelium and stenosis, produces disturbance of ventilation and drainage and thus assists dissemination of the disease. It appears unlikely, however, that small caseous lung foci could lead to massive bronchogenic dissemination. Healing may be rapid or the fistula may remain open for months. The prognosis is favourable if an early diagnosis is made and treatment is begun at once with PAS and streptomycin. Surgical intervention is undesirable.

T. M. Pollock

1273. **Intraabdominal Complications and Sequelae of Pneumoperitoneum**
R. T. Fox, J. R. Thompson, O. L. Bettag, E. S. Gilbert, and W. M. Lees. *Diseases of the Chest* [*Dis. Chest*] **25**, 679–688, June, 1954. 6 figs., 24 refs.

At the Municipal Tuberculosis Sanitarium, Chicago, the authors have studied the necropsy findings in 50 cases of pulmonary tuberculosis treated by pneumoperitoneum. Inflammatory changes were present in the peritoneum, especially that covering the liver and spleen, 45 cases (90%), its extent being proportional to the duration of the pneumoperitoneum. The characteristic appearance was of a translucent pearly grey or pale blue sheet covering the serous surface of the organs involved, with piling up of fibrinous and fibrous material and adhesion to surrounding structures in certain cases, a fibrous perihepatitis sometimes developing of such degree as to deform the liver and shift it from its normal position. These changes were found to be more severe in the visceral than in the parietal peritoneum. Microscopically, the capsule of an affected organ was often thickened. The peritoneum itself showed a covering of fibrous and fibrinous material, a layer of piled-up mesothelium, and a thickened, vascular subserous layer. Photomicrographs are reproduced illustrating these changes, which the authors regard as a local reaction to the intraperitoneal presence of air under pressure.

A brief clinical review of a series of 1,500 patients receiving pneumoperitoneum treatment during the period 1948–52 is included. Two patients died as a direct or indirect result of the treatment, one of whom developed diffuse tuberculous peritonitis originating from caseous tuberculous salpingitis, while the other died from non-tuberculous peritonitis following appendicitis, the signs of which were masked by the pneumoperitoneum. Abdominal symptoms severe enough to necessitate abandonment of the treatment occurred in 15 patients (1%), of whom 6 developed low-grade peritonitis with small-bowel obstruction presenting as paralytic ileus; all responded to medical measures with continuous gastric suction. It is suggested that the pathological changes described above may cause a disturbance of visceral function, of which these 15 cases were examples.

John Taubman

1274. **The Tuberculous Aetiology of Transient Eosinophilic Infiltrations of the Lungs.** (Tuberkulöse Ätiologie flüchtiger eosinophiler Lungeninfiltrate)
E. Lehmann. *Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung* [*Beitr. Klin. Tuberk.*] **111**, 489–500, 1954. 9 figs., 33 refs.

Loeffler's syndrome, a peculiar type of transitory infiltration of the lung associated with eosinophilia, has been variously described as resulting from infestation with certain parasites, as a toxic reaction to certain drugs, foods, and plants, and as a manifestation of infection with various micro-organisms, including the tubercle bacillus. In view of the evanescent nature of the infiltration the possibility of a tuberculous aetiology has generally been rejected. However, the present author describes two cases in which no other aetiological factor could be found, together with a third case in which the differential diagnosis was more difficult, since in addition to tuberculous infiltration of one lung, several transitory areas of infiltration appeared during infestation with *Ascaris* and disappeared after its treatment. The author states that the eosinophilia in cases of Loeffler's syndrome of tuberculous aetiology is less than in cases associated with worm infestation, and suggests that the appearance of these transitory areas of infiltration in tuberculosis is probably the result of a hypersensitivity reaction to tuberculin.

Franz Heimann

1275. **Preliminary Report on the Serial EEGs of Pulmonary Tuberculous Patients Treated with Isoniazid**
D. L. Winfield, P. J. Sparer, and S. Phillips. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **6**, 149–151, Feb., 1954. 2 figs., 5 refs.

Isoniazid in large doses causes excitement and convulsions in animals, and twitching and convulsions have been reported in man after its administration in therapeutic doses. At the Veterans Administration Hospital, Memphis, Tennessee, electroencephalograms were recorded from 52 patients with tuberculosis before and during treatment with 150 to 300 mg. of isoniazid daily. While some of the initial records were abnormal, none, normal or otherwise, was observed to change during treatment.

W. A. Cobb

1276. **A Clinical Report on Isoniazid with Special Reference to Resistance and Liability to Relapse.** (Ein Erfahrungsbericht über INH unter Berücksichtigung von Resistenz und Rezidivhäufigkeit)
D. Groeben and H. J. Neumark. *Tuberkulosearzt* [*Tuberkulosearzt*] **8**, 282–290, May, 1954. 7 figs., 13 refs.

The authors are of the opinion that the results of treatment of pulmonary tuberculosis with isoniazid depend largely on the patient's age, the form of the tuberculosis, the mode of development of the disease, and the probable prognosis. In this paper from the Provincial Hospital, Heiligenhafen-Holst, Germany, they report the results in 505 cases treated with isoniazid for periods ranging from 2 to 10 months (average duration 5 months), the dosage in most cases being 5 mg. per kg. body weight daily. In 28 cases there were temporary side-effects such as fibrillary twitching in the muscles, polyarthritis, petechiae, anorexia, and headache, but these were in no case severe enough to necessitate interruption of the treatment. In 29·5% of the cases the authors noted a reduction in haemoglobin values.

While radiologically the greatest improvement was observed in cases of the proliferative and exudative forms of tuberculosis without cavities, the fibrotic forms showed only an amelioration of the general condition. Exudative forms with cavities also responded well to isoniazid, but resistance to the drug developed after 3 months' treatment in 30% of all cases and after 6 months in 50%. In 146 cases the treatment with isoniazid was combined with surgical measures. In a 12-

month follow-up period of observation of 235 patients who had been discharged from hospital a relapse occurred in 18%. *Franz Heimann*

1277. **The Clinical Effect of Isoniazid and Iproniazid in the Treatment of Pulmonary Tuberculosis**
R. G. BLOCH, A. S. DOONEIEF, A. S. BUCHBERG, and S. SPELLMAN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **40**, 881–900, May, 1954. 3 figs., 6 refs.

The comparative efficacy of isoniazid and iproniazid in the treatment of pulmonary tuberculosis was investigated at the Montefiore Hospital, New York. A total of 114 patients was divided into three treatment groups receiving, respectively, isoniazid alone, isoniazid and streptomycin, and iproniazid alone. Some of these patients had already had chemotherapy. Iproniazid was found to be the most effective drug in alleviating the common symptoms of tuberculosis, but 23 of the 34 patients receiving it developed toxaemia, which was sometimes severe and frequently affected the central nervous system. Sputum conversion was achieved in 13 of the patients in this group. The authors emphasize that iproniazid should be given only to selected patients with pronounced symptoms. [In many sanatoria it is no longer given.] A surprising finding was that the degree of radiological improvement in patients given streptomycin and isoniazid was not greater than that observed in patients receiving isoniazid alone. Toxic effects of isoniazid were not significant, but the authors believe that resistance to the drug developed, although this was somewhat difficult to evaluate. Sputum conversion was noted in only 4 of the 27 patients receiving isoniazid alone, compared with 20 of the 53 receiving streptomycin and isoniazid. All three treatment regimens were found to be effective only in the exudative caseous stage of the disease.
Paul B. Woolley

1278. **Combined Aerosol Treatment with Chemotherapeutic Agents and Hyaluronidase in Pulmonary Tuberculosis.** (Antibiotiques et hyaluronidase associés en aérosols dans le traitement des lésions de tuberculose pulmonaire)
—. WARNERY, G. DUMON, —. BRIN, R. VOISIN, and —. CHANAS. *Revue de la tuberculose* [*Rev. Tuberc. (Paris)*] **18**, 37–45, 1954. 4 figs., 5 refs.

The authors describe the effect of aerosol treatment in 166 cases of pulmonary tuberculosis at the Sanatorium du Petit-Arbois and the Hôpital Sainte-Marguerite, Marseilles. All patients were given two daily treatments, each of about 20 minutes, the nebulized chemotherapeutic agents in the aerosol being dihydrostreptomycin (1 g.) and isoniazid (50 mg.), alone or in combination, and streptomycin and PAS (1 g. of each), together with 150 units of hyaluronidase.

The authors point out that this was in no sense a controlled study, as neither the treatment given nor the cases selected were comparable. Some of the cases were of long standing and had been previously treated medically and surgically, while in others the disease was recent and untreated. The results were assessed principally on the radiological changes, although the clinical state was also taken into account. The most striking improvement was seen in the most recent cases, but in some cases in which collapse therapy had failed aerosol treatment was found to be of value. The cases are divided and subdivided into a large number of groups, but the over-all results were as follows: out of 52 cases of more than one year's standing, 18 were improved; and of 114 cases of less than one year, 82 (72%) were improved, 45 of these being assessed as "very good" and 24 as "excellent". Apart from one attack of acute dyspnoea in several thousand treatments, no untoward effects were observed and no allergic dermatosis developed either in patients or staff.
T. M. Pollock

1279. **Focal Reactions Provoked by Potassium Iodide and Trial Immunization with the Methylic Antigen in Chronic Pulmonary Tuberculosis.** (Réactions focales provoquées par l'iodure de potassium et essai d'immunisation par l'antigène méthylique dans la tuberculose pulmonaire chronique)
H. NOUVION. *Poumon* [*Poumon*] **10**, 191–197, March, 1954. 7 figs., 5 refs.

The author presents a report on the effect of the administration of potassium iodide and methylic antigen together with streptomycin and isoniazid in the treatment of 170 chronic and virtually incurable cases of pulmonary tuberculosis at Champrosay Sanatorium, near Paris. The dosage of potassium iodide was 3 g. daily, and the antigen was given for 15 or 16 days each month in an initial daily dose of 0·25 ml. of dilute antigen; this was increased gradually up to 2 ml. of pure antigen. Isoniazid was given daily and streptomycin every 2 days.

After one year's treatment in a first series of 25 cases, the sputum became negative in 10 cases (40%) and radiological improvement was noted in 16 cases (64%). In a second series of 80 cases, the sputum was negative after 4 to 6 months' treatment in 31% and radiological improvement occurred in 41%. This second series was divided into 4 groups according to the drug treatment given: (1) in the group receiving streptomycin and isoniazid, each given alone and alternately for one month, there was radiological improvement in 52%; (2) in the group given streptomycin and isoniazid together the figure was 42%; (3) in the group receiving streptomycin alone it was 29%; and (4) in the group given isoniazid alone it was 45%. In Group 2 (combined treatment) the sputum became negative in 64% of cases, while the comparable figure for the other groups ranged from 22 to 45%.

A few minor toxic reactions from potassium iodide, such as rhinorrhoea, headache, and eye pains, were noted. The quantity of sputum was also increased. Occasionally the body temperature rose during the first few days of treatment, and if it reached 38° C. (100·4° F.) the potassium iodide was withdrawn and begun again 2 days after the temperature had returned to normal. Radiological improvement was more marked on the whole in cases treated with the addition of potassium iodide and methylic antigen than in the author's other chronic cases treated by chemotherapy alone, although in no case was there complete resolution. *G. M. Little*

Venereal Diseases

1280. **An Outbreak of Pyogenic Penile Ulcers Associated with a Microaerophilic Streptococcus Resembling *Hemophilus ducreyi***

A. LEIBOVITZ. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 203–215, May, 1954. 29 refs.

The author noted an unusually high incidence of penile lesions resembling chancroid among United States troops in Kyushu, Japan, during 1951 and early 1952. No fewer than 2,084 smears from penile lesions were examined during 1951 and 1,219 during early 1952, and in 63% of the earlier specimens and 47% of the later smears pyogenic organisms, including a microaerophilic streptococcus which closely resembled *Haemophilus ducreyi*, were found. In 367 cases in which both smears and cultures were examined, smears were positive for this organism in 45·8% of 825 examinations. In none of the cultures was *H. ducreyi* itself isolated, although in 35·15% the microaerophilic streptococcus was grown. Other pyogenic organisms, including diphtheroid bacilli and staphylococci, were found in many cases. A detailed study of the microaerophilic streptococcus was undertaken and is fully described.

Clinically, the incubation period of the penile ulcers varied from 2 to 10 days but was usually 3 to 5 days. They were situated beneath the prepuce in the majority (65%) of cases. In three-quarters of the cases the ulcer was single, and was in most instances from 3 to 5 mm. in diameter. The lesions were circular, with little or no induration, and those which were larger in size showed soft grey necrotic tissue irregularly disposed on the floor. All the ulcers were moderately tender but did not bleed easily. Moderate adenitis was present in 12% of the cases and was bilateral in about one-quarter of these. The ulcers resembled chancroids, but were less tender, more shallow, and spread more slowly, and the edges were seldom undermined.

Intradermal tests with vaccine of *H. ducreyi* were carried out in 42 cases, with positive results in 14. Autoinoculation tests were negative for this organism and in most instances also for the microaerophilic streptococcus. From the results of this investigation the author concludes that smears from lesions and intradermal tests are of doubtful value in the diagnosis of chancroid.

A. J. King

1281. **The Significance of Bodies Seen in Giemsa-stained Urethral Scrapings in Non-specific Urethritis**

R. R. WILLCOX, E. M. HOWARD, and G. M. FINDLAY. *American Journal of Syphilis, Gonorrhea and Venereal Disease* [*Amer. J. Syph.*] **38**, 216–236, May, 1954. 1 fig., 18 refs.

This report from the School of Pharmacy, London, describes the microscopical findings in the urethral scrapings taken from 250 men with non-specific urethritis, both before and after treatment with antibiotics, and compares them with those in scrapings from the urethral and cervical mucous membrane of 45 female consorts of the patients and in similar scrapings from control groups of subjects not suffering from urethritis but including 108 men recently successfully treated for gonorrhoea. All smears were stained with Giemsa's stain.

In the cases of non-specific urethritis, intra-epithelial granules and intra- and extra-epithelial granular bodies like minute clumps of frog spawn (which the authors term "colonies") were seen in varying proportions of the specimens. Both granules and colonies might stain either red or blue with Giemsa's stain. It was found that the red-staining granules and colonies remained constant irrespective of treatment or of clinical improvement, but the blue-staining granules and colonies greatly decreased in number following successful treatment, increasing again if relapse occurred. Examination of scrapings from the female consorts showed similar colonies and granules in a proportion of the cases. In these cases, however, the structures stained blue did not disappear from the scrapings after treatment as they did in the male patients. Among 80 healthy men in the control groups blue granules or colonies were seen in very few cases. They were seen in about half the cases of recent gonococcal urethral infection, but the incidence declined as the urethra became drier. From this evidence the authors regretfully [but very reasonably] conclude that none of the bodies studied in this investigation are concerned with the causation of non-specific urethritis, but are most probably merely products of inflammation.

A. J. King

1282. **Corticotropin, Cortisone, Thyroid, Testosterone in Syphilitic Interstitial Keratitis**

J. V. KLAUDER and G. P. MEYER. *Archives of Ophthalmology* [*Arch. Ophthal.* (*Chicago*)] **51**, 432–444, April, 1954. 1 fig., 23 refs.

Holding the view that methods hitherto used in the treatment of syphilitic interstitial keratitis have not been successful in preventing industrial blindness in severe cases, the authors have tried corticotrophin, cortisone, thyroid extract, and testosterone, alone or in combination, in the treatment of this condition at the Wills Eye Hospital, Philadelphia. The total number of patients treated was 36, and of affected eyes 56, the disease being mild in 11, moderate in 17, and severe in 28. In some cases all other treatment except mydriatics was withheld during the administration of the above agents for purposes of evaluation, but fever therapy and antisyphilitic drugs were given sooner or later in all cases in the series.

Corticotrophin to a total dose of 450 to 670 mg. over a period of 9 to 15 days was given to 3 patients with the severe form of the disease; there was little, if any, improvement at the end of this period. Subconjunctival

injections of 0·05 ml. of an aqueous suspension of cortisone containing 25 mg. per ml. were then given daily for 3 days to 2 of these 3 patients and to 4 others, a further course of 3 injections being given after several days' rest. There was no noticeable improvement, although only one of the 6 patients receiving cortisone in this way had a recurrence after subsequent treatment by other means. In 13 cases cortisone acetate in a concentration of 25 mg. per ml. in a buffered phosphate solution, with 1 in 5,000 benzalkonium chloride as a preservative and spreading agent, was used for local instillation, one drop being instilled into the conjunctival sac hourly during the day and 2-hourly during the night. In mild and moderate cases there was a dramatic clearing of the cornea and subsidence of the inflammation within 7 to 12 days, but in 9 of the 13 cases there was a recurrence on cessation of this treatment which was not prevented by the antisyphilitic therapy then being given. Since the basal metabolic rate was found to be uniformly low, desiccated thyroid, in a dosage of 2 to 3 grains (0·13 to 0·2 g.) daily, was given in the remaining 17 cases and also in 12 of the cases previously treated with cortisone. Administration was continued until improvement was noted, which was generally a few weeks to 2 months, and it is suggested that this treatment enhances the effect of fever and chemotherapy. Three patients received an intramuscular injection of 25 mg. of testosterone *cyclo*pentylpropionate each week for 6 weeks (in addition to other treatment) with little benefit.

The authors believe that some mechanism in the cornea, in all probability an immunological process in which vascularization is concerned, is responsible for regression of the disease, and that until the whole cornea has become vascular and the vessels meet in the centre (crisis), recovery will not take place. Cortisone does not assist this process, but retards it, and the authors have therefore discontinued its use. *Douglas J. Campbell*

1283. **Non-gonococcal Urethritis**

P. Durel, V. Roiron-Ratner, A. Siboulet, and C. Sorel. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **30**, 69–72, June, 1954. 6 refs.

The authors report that their experience of urethritis at the St. Lazare and Cochin Hospitals, Paris, over the last 3 years shows that the incidence has increased, and that cases of non-gonococcal are now more frequent than those of gonococcal origin—1,195 and 805 respectively in a recent series of 2,000 cases. Extensive studies were undertaken, therefore, of the possible causes of the non-specific infections.

The presence of *Trichomonas vaginalis* could seldom be established by direct smear and dark-field illumination alone, and the authors prefer staining by the May–Grünwald–Giemsa method. In some cases examination of 3-day cultures of the organism on 4 ml. of minced meat to which had been added 250 units per ml. of penicillin (*p*H 6·3 to 6·8) proved more accurate than direct smear. *T. vaginalis* was found in 35 of 288 cases. Contacts were frequently found to be carriers of the trichomonad. Cultures for pleuropneumonia-like organisms (P.P.L.O.) were made by transferring a urethral swab into 0·5 ml. of peptonized broth until a culture could be set on Dienes's medium. Positive cultures of the "L" type resulted in 85 cases out of 631. The fact that examination of cultures from 357 healthy individuals gave positive results in 196 cases, however, indicates the need for caution in interpreting such results in the absence of adequate controls.

A search was also made for inclusion bodies in urethral scrapings, which were fixed in methyl alcohol and stained with Giemsa (Kuhlmann) stain for 15 minutes; decolorization with acetone was avoided when possible as it causes blurring. Positive findings were recorded in 28 out of 691 cases. The authors were disturbed to find that usually only one or two cells showed inclusion bodies, whereas in other infections due to the psittacosis group of viruses these bodies are very numerous.

Treatment with aureomycin or "terramycin" (oxytetracycline), as for inclusion gonorrhoea, appeared to be satisfactory for infection with P.P.L.O. In cases of *T. vaginalis* infestation local urethral treatment with aureomycin ointment or "conessine" jelly followed by irrigation with a mixture of potassium permanganate and mercury oxycyanide was used; in exceptional cases instillations of silver nitrate were given. The social importance of non-specific urethritis is discussed.

V. E. Lloyd

1284. **Non-specific Urethritis. Is Mycotic Infection Important?**

G. Auckland and W. J. Preston. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **30**, 81–87, June, 1954. 9 figs., 16 refs.

In the course of one year the authors have found mycotic infection in 36 out of 602 male patients attending Manchester Royal Infirmary for the treatment of non-specific urethritis; in 30 cases no other cause for the urethritis could be established. The fungus, seen as spores or mycelium, was identified in Gram-stained films of urethral or prostatic secretion or in cultures on Sabouraud's medium. The various strains grown included *Candida albicans*, *C. krusei*, *Penicillium*, white yeast, *Rhodotorula*, *Aspergillus*, and *Monilia sitophila*, and the presence of these was not thought to have been due to air-borne contamination of the cultures. About half the patients had previously received treatment with antibiotics. Five cases are described in detail.

The authors discuss at some length the significance which should be attached to the presence of fungus elements in the genito-urinary secretions. These elements are sometimes found in symptomless patients undergoing post-treatment tests for gonorrhoea, and sometimes in patients who have attended only for advice. Occasionally they are found only at infrequent intervals and the reason for this is not clear, but it is possible that the almost universal use of antibiotics may be responsible, since it is known that these drugs upset the balance of the normal flora and so tend to encourage the growth of fungi. If these last are indeed shown to cause infection of the genito-urinary tract, a reclassification of pathogenic and non-pathogenic fungi may become necessary. *V. E. Lloyd*

Tropical Medicine

1285. **The Therapeutic Effect on a Group of Sleeping Sickness Patients of a Single Injection of 3854 R.P. (Mel B Friedheim—Arsobal Spécia)**
A. R. PINTO. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **3**, 464–465, May, 1954. 2 refs.

This preliminary report deals with the effect of " arsobal " (" 3854 R.P.", " Mel B "), given parenterally in a single dose of 4 mg. per kg. body weight, on a group of 16 patients in the first stage of sleeping sickness in Portuguese Guinea. The dose was well tolerated except by one patient, who experienced transient abdominal pain immediately after its administration. There was usually a slight eosinophilia starting 24 hours after the injection and increasing during the following days, which in some cases persisted for as long as one month.

Trypanosomes disappeared from the blood within 24 hours, and were absent from lymph-node fluid and thick blood smears examined a month later. Blood cultures from a number of patients whose cerebrospinal fluid showed an increase in cell and protein content at one month were also negative. On further examination 4 and 8 months after treatment both clinical and parasitological findings were still negative, while the cell and protein content of the cerebrospinal fluid had fallen in all but 4 cases. All patients had albuminuria, mostly slight, before treatment, but 8 months after treatment only 7 still showed traces of albumin in the urine.

The study is being continued. *I. M. Rollo*

1286. **The Treatment of Leprosy with Thiosemicarbazone**
C. W. J. MORRIS. *Leprosy Review* [*Leprosy Rev.*] **25**, 73–77, April, 1954. 5 refs.

Current opinion on the value of the thiosemicarbazones in the treatment of leprosy is reviewed and reference made to the occasional occurrence of agranulocytosis, which the author considers to be an allergic rather than a toxic effect of these drugs. In 1951 " quite a number " of the patients at the Oyi River Leprosarium in Nigeria were found unable to tolerate diaminodiphenylsulphone in the higher doses, and it was decided to treat 18 of these and 20 new, untreated cases with " neustab " (thiacetazone) by mouth. Of these 38 patients, 37 completed the 9-month course, the disease in 20 cases being lepromatous and in the rest tuberculoid, simple macular, or indeterminate in type. The dosage was increased gradually from 12·5 to 150 mg. daily in a single evening dose. Clinically, all the patients showed improvement, which was " marked " in 19, " moderate " in 13, and " slight " in 5. One lepromatous case became bacteriologically negative in this short period, and one patient who had concurrent pulmonary tuberculosis became sputum-negative and afebrile. Mild lepra reactions occurred in 15 cases and more severe lepra reactions in 2 others. The usual fall in haemoglobin level during treatment was readily combated with ferrous sulphate by mouth. The conclusion is drawn that the thiosemicarbazones are useful as " a second arrow for the pharmaceutical bow in the battle against leprosy ".

Clement Chesterman

1287. **Kwashiorkor and Marasmus in Jamaican Infants**
D. B. JELLIFFE, G. BRAS, and K. L. STUART. *West Indian Medical Journal* [*W. Indian med. J.*] **3**, 43–55, March, 1954. 5 figs., 22 refs.

The clinical features and treatment of kwashiorkor and marasmus in Jamaican children of predominantly African extraction are described. The social and economic factors which lead to the development of kwashiorkor in children in equatorial Africa are also to be found in Jamaica: families are large, protective foods are scarce and expensive, the parents are poor, and often ignorant of what the soil can produce for the developing child.

In 31 Jamaican children aged 6 to 31 months the onset of the disease was gradual after weaning, and was usually marked by a period of diarrhoea which had persisted for a few weeks to a few months before the child was admitted to hospital. The patients were divided into three groups according to the clinical picture as follows: (1) 18 patients with kwashiorkor distinguished by dermatosis, oedema, hypochromotrichia, cheilosis, and glossitis, with muscle wasting but no great loss of subcutaneous fat; (2) 9 patients with marasmic kwashiorkor, that is, with minimal mucocutaneous lesions but more muscle wasting and more loss of fat than in patients of Group 1; and (3) 4 patients with marasmus characterized by severe wasting of muscle and subcutaneous fat, dehydration, and absence of the characteristic epidermal lesions. Although there was some overlapping between the syndromes, there was a good deal of difference between them in response to treatment.

Liver biopsy was performed in all cases. Fatty change, most marked in cells at the periphery of the lobule, was noted in all cases and was severe in the kwashiorkor group. Haematological examination, which included a blood count and estimation of the plasma protein level, yielded results by now familiar to students of this disease in other parts of the tropics. The reaction to the thymol turbidity test was positive, and the serum cholinesterase level was low in all cases. Treatment consisted primarily in administration of skimmed milk by mouth or by intragastric tube. Dehydration, when present, was corrected by intravenous or subcutaneous administration of Hartmann's solution, and anaemia by blood transfusion and, later, by oral administration of ferrous sulphate. The results of treatment were good. Only 2 patients died, one of them being moribund on admission and the other, with marasmus, dying after several months from enteritis due to a drug-resistant strain of *Salmonella*. [The paper includes excellent photographs, which demonstrate the value of the milk treatment.] *William Hughes*

Allergy

1288. **The Risk of Shock in Percutaneous Administration of Allergens. Report of a Case of Sudden Death in Connection with Specific Desensitization.** [In English] E. B. SALÉN and R. BJÖRNSTJERNA. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] 7, 306–325, 1954. 9 refs.

From a review of reports in the literature of cases in which patients have died after intradermal skin testing the authors conclude that although shock reactions due to various causes occur not infrequently during specific desensitization, death is very rare. They then describe the case, occurring at Södersjukhuset, Stockholm, of a 13-year-old boy who died suddenly of anaphylactic shock following a subcutaneous injection given during a course of rapid hyposensitization to dog and horse scurf. The patient had had an attack of asthma on the night before his death which might have been related to an injection of dog allergen. On the day of his death the same dose of dog allergen was given at 10.30 a.m. without ill effect. At 8.30 a.m. he had had a dose of horse allergen (0·4 ml.), and at 1 p.m., as he was quite well, he received an injection of 0·6 ml. of the same extract. He remained apparently well and active for over 2 hours, but at 3.30 p.m. sneezing, itching of the skin, and severe dyspnoea suddenly set in and in spite of immediate and energetic treatment the boy was dead within 15 minutes. Post-mortem examination showed the lungs to be in maximal expansion and exhibiting the histological changes usually seen in acute asthma. The causes of anaphylactic shock and methods for its prevention, including the administration of ACTH or cortisone, are discussed in detail. *A. W. Frankland*

1289. **Prophylaxis of Summer Hay-fever and Asthma. A Controlled Trial Comparing Crude Grass-pollen Extracts with the Isolated Main Protein Component**
A. W. FRANKLAND and R. AUGUSTIN. *Lancet* [*Lancet*] 1, 1055–1057, May 22, 1954. 9 refs.

A comparative controlled investigation of crude pollen extracts and the purified main protein component of such extracts in the prophylaxis of summer hay-fever, with and without associated asthma, is reported from St. Mary's Hospital, London. Of 200 patients, 57 of whom had summer asthma, 100 received injections of grass pollen (50 having the standard crude pollen extract ("pollaccine") and 50 a purified pollen extract), 50 were given injections of phenol–saline solution, and 50 received an inactive ultrafiltrate prepared in the process of concentrating the active material in the pollen extract. The patients were chosen at random to permit statistical analysis, and the groups were comparable in all respects.

The patients kept a daily record of their symptoms, and after the course of treatment was completed the results were recorded in ignorance of the particular preparation injected. The pre-seasonal pollen treatment consisted in a single course of injections to a total of 20,000 Noon units. Results were "excellent" or "good" in 78 of the 100 patients so treated, 26 being completely free from hay-fever. Of the 100 patients receiving injections of phenol–saline solution or ultrafiltrate, the results were "excellent" or "good" in 33, but only one patient claimed to be completely free from symptoms. Pollen injections were given to 31 of the 57 patients with asthma, results being "excellent" or "good" in 29; of the remaining 26 who received phenol–saline solution or ultrafiltrate, only 8 responded well. The probability that the difference between the two groups given specific treatment or inactive material was due to chance was found to be less than 1 in 1,000.

General reactions to treatment occurred in 30 of the pollen-treated patients. The reaction to the skin test was smaller after injection of pollen extract than it was before treatment started; there was no change in the size of the weal in patients given phenol–saline solution or ultrafiltrate. The results obtained with the usual crude pollen extract and with the main protein component were similar and equally good, suggesting that other protein fractions are not significant.

[This controlled investigation is a model for future trials, since it permits comparison between various agents in specific treatment and between such treatment and the effect of injection procedures *per se*.]

J. Pepys

1290. **Maintenance Cortisone in Intractable Asthma. Preliminary Observations of Undesirable Cortisone Effects**
J. W. IRWIN, P. H. HENNEMAN, D. M. K. WANG, and W. S. BURRAGE. *Journal of Allergy* [*J. Allergy*] 25, 201–209, May, 1954. 4 figs., 4 refs.

In 23 cases of perennial severe asthma of undetermined aetiology seen at Massachusetts General Hospital the symptoms were brought under control by the parenteral or oral administration of cortisone in high doses. Then the dosage was gradually decreased until symptoms reappeared, so enabling a maintenance dose to be established at a slightly higher level. In 12 of these patients the maintenance dose was 62·5 or 75 mg., while in the others it varied between 50 and 150 mg.

In this way many of these patients have been maintained without symptoms for 3 years. All of them developed some minor side-effects such as "moon face", facial hair, or acne, and all but one gained weight, some of them considerably, but diabetes, oedema, hypertension, and potassium deficiency did not occur. One patient developed marked hypercalciuria and showed evidence of osteoporosis, calcium output falling to normal when cortisone was stopped and rising again when it was resumed. In 5 other cases a high urinary calcium content was repeatedly found, but there was no evidence of osteoporosis. *H. Herxheimer*

Nutrition and Metabolism

1291. **Utilization of Intravenously Injected Fructose and Invert Sugar in Normal Human Subjects**
I. H. STRUB, W. R. BEST, C. F. CONSOLAZIO, and M. I. GROSSMAN. *Journal of Clinical Nutrition* [*J. clin. Nutr.*] **2**, 32–37, Jan.–Feb., 1954. 3 figs., 22 refs.

Nine normal male subjects each received the following intravenous infusions lasting 3 hours each on 3 separate days: 141 g. of glucose, 291 g. of fructose, and 288 g. of invert sugar. The mean highest total blood sugar concentrations were 187 mg. per 100 ml. for the glucose infusion, 191 mg. per 100 ml. for the fructose infusion, and 242 mg. per 100 ml. for the invert sugar infusion The urinary loss of total sugar (glucose plus fructose), expressed as per cent of sugar infused, was 2·1% for glucose infusion, 6·2% for fructose infusion, and 5·0% for invert sugar infusion. Although under the conditions of this study it was found that in normal subjects the percentage urinary loss is slightly greater for fructose infusions than for invert sugar infusions, there is a possibility that fructose might have specific advantages, other than providing calories, in certain clinical conditions because of its distinctive metabolic effects.—[Authors' summary.]

1292. **Maturation of Bone Centers in Hand and Wrist of Children with Chronic Nutritive Failure. Effect of Dietary Supplements of Reconstituted Milk Solids**
S. DREIZEN, R. M. SNODGRASSE, G. S. PARKER, C. CURRIE, and T. D. SPIES. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **87**, 429–439, April, 1954. 2 figs., 7 refs.

Continuing their previous work on the effect of a dietary supplement of reconstituted milk solids on skeletal maturation in children with nutritive and growth failure (*Amer. J. Dis. Child.*, 1953, **85**, 1; *Abstracts of World Medicine*, 1953, **14**, 163), the authors have studied the differential utilization of the nutrients in the milk by bone centres in a selected skeletal area. At the Jefferson-Hillman Hospital, Birmingham, Alabama, 164 children, aged 1 to 15 years, with defective bone formation as a result of unsatisfactory diet, were paired according to sex, age, and the condition of the bones. Ossification centres in the left hand and wrist, 28 in all, were examined radiologically. Milk supplements varying from 3 to 12 [U.S.] quarts (2·8 to 11·4 litres) a week were given to half the children for 6 to 40 months; the other half did not receive extra milk. Radiographs were taken at the beginning and end of different treatment periods, and the rate of maturation of the bones was assessed by Todd's method.

Radiographs showed that prolonged nutritive failure affected the ossification centres in different degrees; the mid and distal phalanges were most retarded and the capitate and hamate bones the least. The degree of retardation increased with age. The milk supplements accelerated the over-all rate of maturation but did not affect all bones equally, the greatest response being observed in the fastest-growing centres and the smallest in the slowest-growing bones. *H. E. Magee*

1293. **Clinical Observations on Sporadic Cases of Scurvy in Adults. I. Haematological Aspects. II. Endocrinological Aspects.** (Osservazioni cliniche su alcuni casi di scorbuto sporadico degli adulti. Considerazioni ematologiche. Considerazioni endocrinologiche)
F. BERTOLANI and G. CHIEREGO. *Minerva medica* [*Minerva med.* (*Torino*)] **1**, 1173–1185, April 28, 1954. 13 figs., bibliography.

The authors describe 14 sporadic cases of scurvy seen at the University Medical Clinic, Modena, since 1946. The diagnosis of scurvy in these patients was made on the basis of clinical signs; in some cases, in addition, low ascorbic acid levels were found in the blood and lowered excretion in saturation tests.

The haemorrhagic symptoms are well illustrated in the colour photographs which accompany the paper. Most of the cases showed a considerable degree of anaemia, which was hypochromic in 2 cases, normochromic in 7, and hyperchromic and macrocytic in 5. In 2 patients with megaloblastic anaemia bone-marrow biopsy showed normoblastic haematopoiesis with constant marrow hyperplasia. In some cases the anaemia appeared to be refractory to treatment with ascorbic acid alone, but in all cases the erythrocyte count became normal when iron, liver extract, and vitamins of the B complex were added. [No further details about treatment are given.] The pathogenic factors involved in the causation of the different types of scorbutic anaemia are discussed at some length, with special reference to the need of ascorbic acid for the conversion of folic acid to folinic acid.

The endocrinological aspects of scurvy are then considered, and the authors suggest that the disease may have some relation to the functions of the gonads, adrenal cortex, and pituitary gland. They note that only one of their 14 patients was a woman and that most of the patients described in the literature have been males. The majority of their patients had reduced sexual activity, and in 2 cases 17-ketosteroid excretion was markedly reduced. They go on to suggest that the muscular asthenia, adynamia, reduced resistance to fatigue, apathy, feeling of cold, and hypotension seen in their patients could be attributed to the effect of scurvy on the adrenal glands. After administration of ACTH the reduced 17-ketosteroid excretion rose considerably, and became nearly normal after treatment with ascorbic acid. There were also slight changes in the blood electrolyte concentrations after treatment. Similarly, there were noticeable changes in the eosinopenic response to ACTH after administration of ascorbic acid. *Z. A. Leitner*

1294. **Particulate Fat Absorption and Secretion**
H. SINGER, J. SPORN, and H. NECHELES. *Gastroenterology* [*Gastroenterology*] **26**, 299–302, Feb., 1954. 1 fig., 19 refs.

In experiments performed at the Michael Reese Hospital, Chicago, coconut oil and olive oil were introduced into a Thiry fistula loop in 3 dogs. The loop contents contained no bile, the lipase concentration was 40 to 80 units per ml., and the *p*H was 6·1 to 6·3. The fat was finely emulsified in the Thiry loop, and the occurrence of particulate absorption was shown by chylomicrographs, which showed a peak increment between the second and third hours of the experiment. Fine particles were also observed in the fasting contents of these loops. These particles were not affected by antibacterial agents, and were thought to be secreted fat particles. [No analytical data are given.]

[Contrary to the authors' statement, these observations are *not* incompatible with the partition hypothesis of fat absorption.] *A. C. Frazer*

1295. **Effect of Age on the Utilization of Various Carbohydrates by Man**
A. A. ALBANESE, R. A. HIGGONS, L. ORTO, A. BELMONT, and R. DILALLO. *Metabolism* [*Metabolism*] **3**, 154–159, March, 1954. 2 figs., 9 refs.

At the Nutritional Research Laboratory, St. Luke's Hospital, New York, the blood sugar level was determined at intervals on a number of fasting subjects ranging in age from 5 to 89 years after a dose (1 g. per kg. body weight) of dextrose, fructose, sucrose, or lactose in 250 ml. of water had been given by mouth. In addition, urine was collected for the 24 hours following the test dose and was assayed for sugars.

Calculation from the results obtained suggested that the utilization of dextrose (glucose) was considerably depressed with increasing age, whereas the utilization of fructose was only slightly affected. Sucrose and lactose occupied intermediate positions. That this effect was not due to a relative insulin deficiency in old age was shown by the finding that, even in diabetics satisfactorily controlled with insulin, dextrose caused a far greater elevation of blood sugar than did fructose. It is therefore suggested that fructose and fructose-containing products are the sugars of choice in nutrition of the aged. *G. A. Smart*

1296. **Depletion of Potassium Induced in Man with an Exchange Resin**
P. FOURMAN. *Clinical Science* [*Clin. Sci.*] **13**, 93–110, Feb., 1954. 7 figs., 37 refs.

Previous studies of potassium deficiency have mostly been made on patients suffering from some other disease condition. From the Nuffield Department of Clinical Medicine, Oxford, the author reports three experiments on 2 healthy adults, one woman and one man, in whom deficiency of potassium was induced by giving a sulphonated polystyrene exchange resin (" zeokarb 225 ") in the hydrogen or ammonium form in the diet, which supplied 1,600 to 2,500 Cal. per day and contained only 31 to 38 mEq. of potassium, with supplements of sodium salts. Changes in blood electrolyte and nitrogen levels and in excretion of water, acid, and ammonium were determined for 8 days before giving the resin, during the treatment, and, in two experiments, for 8 and 12 days respectively afterwards. The resin was given in a dose of 60 g. daily for 8 days, followed by 90 g. per day for 4 days in one experiment and for 8 days in the other two experiments. The urine was analysed in 2-day periods and the faeces in 4-day periods, and blood was withdrawn for analysis from time to time. After the experiments were completed the total body water was estimated in both subjects by the antipyrine method.

The clinical changes which occurred were more obvious during treatment with the ammonium-charged resin, and consisted in muscle weakness, anorexia, thirst, sensitivity to cold, mental changes ranging from irritability to apathy and stuporose confusion, dyspnoea on exertion, constipation, and vomiting. After the resin was stopped the subjects were still morose, easily tired, and ill-looking.

The resin absorbed more potassium than was in the diet and some must have come from intestinal secretions, while the urinary excretion of potassium continued in spite of the mounting deficit. Obvious symptoms appeared when 360 to 430 mEq. of potassium had been lost, or 15% of the total body content, and the total loss in the three experiments was 340, 670, and 840 mEq. respectively, the last two figures representing about 28% of the total body potassium. The smallest loss occurred with the hydrogen-charged resin. The serum potassium level fell in two experiments, but remained unchanged in the subject who was most ill. Loss of water, nitrogen, and phosphate from cells was proportionately much less than loss of potassium. While the ammonium resin was being given no sodium, magnesium, or calcium was retained in place of potassium, but during administration of the hydrogen-charged resin sodium equivalent to the potassium lost was retained, and the serum sodium level rose. The loss of potassium was accompanied by an extracellular acidosis, and the plasma bicarbonate levels fell to 17, 12, and 15 mEq. per litre. There was an increase in urinary ammonia and titratable acidity. While the hydrogen-charged resin was being given 238 mEq. of chloride and 0·5 litre of water were retained, but the plasma chloride level fell, indicating a transfer of water from cells to the extracellular fluid. During administration of the ammonium resin sodium, chloride, and up to 3 litres of water were lost. Sodium and water entered the cells only during the last 4 days of the 16-day experimental period.

During the recovery phase the rate of correction of the potassium deficiency was limited by the amount available in the diet. Sodium was retained in excess, at first to enter the cells and later to augment the extracellular fluid, so that on the 9th day of recovery the female subject developed oedema. The acidosis was soon corrected and the plasma bicarbonate level rose above the control values, the male subject developing tetany with a urinary excretion of calcium of only 20 mg. per day. As the acidosis was corrected, water and phosphate reentered the cells. The deficit of nitrogen was not corrected during the recovery period in spite of an adequate intake of protein. *Thomas B. Begg*

Gastroenterology

1297. **Emergency Treatment of Bleeding Esophageal Varices. Treatment by Transesophagoscopic Sclerosing Injection plus Pneumatic Tamponade**
E. D. PALMER. *Archives of Otolaryngology* [*Arch. Otolaryng. (Chicago)*] **59**, 536–542, May, 1954. 3 refs.

The aim of the emergency treatment of bleeding oesophageal varices, as practised by the author at the Walter Reed Army Hospital, Washington, D.C., is to control the haemorrhage until portal decompression, preferably by porta-caval shunt, can be carried out, experience having shown that this is not practicable while active bleeding continues. The transoesophageal injection of sclerosing agents, which has largely been superseded by the shunt method as a definitive treatment of this condition, can be carried out as an immediate measure at the time of diagnostic oesophagoscopy. In some cases, however, histological examination fails to show any evidence of thrombosis following injection, and it is suggested that in addition to the induction of venous stasis by pressure at the cardia before injection to encourage retention of the sclerosing fluid, apposition of the walls of the varix by pneumatic tamponade after injection should make the method more effective.

The technique adopted by the author in cases of acute haemorrhage from oesophageal varices is described. Immediately on admission blood transfusion is started and the stomach thoroughly washed out with ice water. Oesophagoscopy is then performed, a Sengstaken tube passed, and the varices injected with the gastric balloon pulled up against the cardia. As soon as the injection is completed the oesophagoscope is withdrawn and the oesophageal balloon inflated, this procedure taking about 20 seconds. The Sengstaken tube is left *in situ* for at least 5 days, with continuous manometric control of the balloon pressure. It is pointed out that control of the bleeding is urgently necessary in these cases not only on account of the loss of blood, but also to prevent the failure of liver function which, if blood is freely available for transfusion, is a greater danger than exsanguination in the author's experience.

F. W. Watkyn-Thomas

1298. **A Comparison of the Effects of Acetyl-beta-methylcholine Chloride (Mecholyl) on Esophageal Intraluminal Pressure in Normal Persons and Patients with Cardiospasm**
N. C. HIGHTOWER, A. M. OLSEN, and H. J. MOERSCH. *Gastroenterology* [*Gastroenterology*] **26**, 592–600, April, 1954. 3 figs., 12 refs.

Some observations on the action of acetyl-beta-methylcholine (" mecholyl ") upon the muscle of the oesophagus in patients with cardiospasm and in healthy subjects are reported in this paper from the Mayo Clinic. Pressure developed at the junction of the middle and lower thirds of the oesophagus was recorded by means of an electric pressure transducer on 15 patients with cardiospasm, 4 with scleroderma, benign stricture of the oesophagus, or oesophageal spasm, and 10 healthy subjects. After a 6-hour fast pressure in the resting oesophagus was measured for 20 minutes, and then the response to swallowing water and solid food was recorded. All the subjects were given 10 mg. of mecholyl subcutaneously, and pressures were recorded for another 30 minutes.

In patients with cardiospasm the pressure developed in response to swallowing was only 20% of that developed in healthy subjects; this, however was not specific to cardiospasm, because it was observed also in the patients with other oesophageal lesions. After administration of mecholyl the resting pressure in the oesophagus of healthy subjects rose by 10 cm. of water, the rise beginning within 3 minutes and ceasing in less than 20 minutes. In patients with cardiospasm the rise in pressure was 20 cm. of water and lasted somewhat longer than 20 minutes; 10 of these experienced substernal pain after the injection of mecholyl, but this was not observed in the healthy subjects. The 4 patients with oesophageal lesions but no cardiospasm did not respond abnormally to mecholyl. The authors suggest that the exaggerated response to parasympathicomimetic drugs in patients with [so-called] cardiospasm may indicate an absence of normal parasympathetic nerve supply to the oesophagus.

A. G. Parks

1299. **Prefrontal Infiltration with Procaine in Digestive Disorders.** (L'infiltration novocaïnique préfrontale en pathologie digestive)
R. CATTAN, P. FRUMUSAN, and M. BUCAILLE. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. Appar. dig.*] **43**, 137–158, Feb., 1954. 4 figs., 6 refs.

The authors describe, from the Hôpital Saint-Antoine, Paris, 4 cases in which gastrointestinal lesions of considerable severity dramatically improved after infiltration of the prefrontal area of the brain on both sides with procaine hydrochloride. This technique was devised by the third-named author and has been used in more than 50 other cases, mainly of inoperable cancer, for the relief of intractable pain. It is claimed that it is as effective as, and far less traumatic than, other neurosurgical methods such as lobotomy. The aim is the interruption of the pathways from the frontal cortex to the thalamus without damage to the cortex itself, and to achieve this 15 ml. of 1% procaine is first injected under pressure, after careful radiological location, into one frontal lobe, the procedure being repeated a few days later on the other side.

The first patient, a man of 67, was crippled by severe polyarthritis and suffering very intense pain. When treated with cortisone for the arthritis he developed severe rectal haemorrhages, which were found to come from diverticula of the sigmoid colon. The cortisone

had therefore to be abandoned, whereupon the arthritic pains returned and it was because of the intractable nature of these that bilateral prefrontal infiltration was carried out. This procedure not only relieved the joint pain, but the rectal bleeding also ceased and has not recurred for one year. The second case was that of a woman aged 22 who was suffering from a severe recurrence of haemorrhagic proctocolitis and who had shown no improvement following a multitude of treatments. Bilateral prefrontal infiltration was performed and the improvement in both the amount of bleeding from the bowel and the general condition of the patient that immediately followed was dramatic, the sigmoidoscopic appearances becoming almost normal within one week. The third case was one of severe haemorrhage from a duodenal ulcer; this ceased abruptly after infiltration. The last patient was a man of 74 with a giant ulcer of the lesser curve of the stomach. He was in great pain and showed no improvement after 6 weeks' treatment in hospital. Bilateral infiltration was carried out, when the pain was immediately relieved and the ulcer healed rapidly.

The authors frankly discuss the possibility that these results were due to coincidence, and they analyse the possible mechanism by which such infiltration might affect the gastrointestinal tract.

[Those interested in this technique should consult the original, which contains case histories and a discussion of the points involved.] *T. D. Kellock*

1300. **Benign Gastroduodenal Disorders Treated by Billroth-I Gastric Resection**

E. J. SCHMITZ, H. N. HARKINS, H. G. MOORE, and H. H. OLSON. *Lancet* [*Lancet*] **2**, 4–9, July 3, 1954. 3 figs., 21 refs.

At King County Hospital (University of Washington School of Medicine), Seattle, between January, 1948, and June, 1953, 198 patients were subjected to the operation of subtotal gastrectomy (by the Billroth-I technique) for benign gastroduodenal disorders. The lesions present were mainly chronic or acute gastric or duodenal ulcers, but in 2 instances nothing abnormal was detected in the excised portion of the stomach, while in 2 others the only lesion found was gastritis. The average age of the patients was 55·5 years; 32 of them suffered from cardiovascular disease and 39 from severe chronic alcoholism. Usually seven-tenths of the stomach was removed and an end-to-end union of stomach and duodenum performed; in a few cases the union was end-to-side. Interrupted silk sutures were used for both rows of sutures; only rarely was a continuous catgut suture used for the deep layer. There were 6 deaths, in patients aged respectively, 63, 66, 67, 74, 75, and 77. Patients were got out of bed and induced to walk on the first postoperative day, and the average stay in hospital after operation was 11·9 days. There were postoperative complications in 42 cases. After a brief follow-up the authors classify the results as " excellent " in 109 cases, as " satisfactory " in 58, and " poor " in 15 (including the 6 deaths). It is pointed out, however, that 109 of the patients were observed for no more than a year, and 48 for 3 months or less. *Zachary Cope*

1301. **Stellate Angiomata in Hepatic Diseases.** (О так называемых сосудистых звездочках при болезнях печени)

G. N. KARAPETYAN. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **32**, 44–47, Feb., 1954.

The diagnostic value of stellate or " spider " angiomata in hepatic cirrhosis has been recognized for many years. Tareev considered them of great importance in liver disease as indicating the onset of cirrhosis, and attributed their formation to loss of tone in the cutaneous vessels as a result of toxic effects; he believed that they also occur on the mucous membrane of the oesophagus and stomach and can be recognized by gastroscopy; in that situation, they may form a focus of haemorrhage. They occur at a number of different sites in the upper half of the body, are usually fairly small in size, but may attain greater dimensions and form an angioma as large as a bean. They have a central vessel about the size of a pin's head, and pressure on the central part causes the angioma to fade, while pressure on the periphery has no effect, showing that they are of arterial origin.

The present author has seen them in 2 cases of infective hepatitis which showed other evidence of early cirrhosis. He cites Konovalov as describing similar vascular formations in hepatolenticular degeneration. In the author's opinion these angiomata are part of a general atonia of the peripheral blood vessels due to the action of histamine-like substances which are formed as a result of impairment of hepatic function; they may at first be a reversible phenomenon, but in the later stages of hepatic impairment they become permanent. He suggests that it is largely to similar effects on the cerebral vessels that the changes which occur in the central nervous system in serious hepatic disease must be attributed.

L. Firman-Edwards

1302. **Diarrheal Syndrome. Report on Therapy Using Resion with Polymyxin and Phthalylsulfacetamide**

J. WEISS. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] **22**, 64–72, July, 1954. 21 refs.

Although resion, which contains a polyamine anion-exchange resin, sodium aluminium silicate, and magnesium silicate, is claimed to be effective in the treatment of many forms of diarrhoea, the present authors have not found it consistently so, especially in the control of diarrhoea caused by antibiotics. Polymyxin and phthalylsulphacetamide were therefore added to resion in the hope that this combination of drugs would control fungal and bacterial infections of the gastrointestinal tract. All of 12 patients with the antibiotic diarrhoeal syndrome derived benefit within 24 hours, cramp-like pains being relieved and the diarrhoea being controlled after an average period of 5 days. Of 10 patients with ulcerative colitis 9 improved, diarrhoea being controlled within 5 days of the start of treatment. Patients with summer diarrhoea [the aetiology of this is not stated, though all the patients were adults] also responded to this treatment, the majority obtaining relief of symptoms within 36 hours. It is concluded that this form of treatment " approaches the ideal " for these and similar diarrhoeal syndromes. *K. Gurling*

Cardiovascular System

1303. **Radiocardiography in Congenital Heart Disease**
D. GOLDRING, H. M. ROGERS, M. TER-POGOSSIAN, W. SEAMAN, and M. R. BEHRER. *Journal of Pediatrics* [*J. Pediat.*] **44**, 392–406, April, 1954. 12 figs., 9 refs.

A preliminary study was made at the St. Louis Children's Hospital (Washington University School of Medicine) of the use of radiocardiography in the diagnosis of congenital heart disease, but no definite conclusions could be reached. In the technique described, which was used on 22 normal children and 100 with congenital heart disease, diiodofluorescein labelled with radioactive iodine (^{131}I) is injected intravenously and a Geiger counter placed over the midsternal line at the level of the 4th interspace, the output of which is fed into a recording device. A curve is thus obtained, the form of which was fairly constant in normal subjects, but which showed certain differences in the various forms of congenital heart disease. The physiological explanation of these varying patterns eludes the authors, but it is thought that the radiocardiogram is predominantly a reflection of blood flow in the right heart. *James W. Brown*

1304. **Cardiac Involvement in Hemochromatosis**
H. P. LEWIS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 544–558, May, 1954. 6 figs., 22 refs.

Haemochromatosis is a rare disease and its presence is often only recognized at necropsy. Its manifestations are varied: it may occur without causing pigmentation or diabetes, and it may present primarily as a cardiac disease; it is this aspect of the condition which is discussed in this paper from the University of Oregon Medical School.

The excessive storage of iron which occurs in haemochromatosis may come about in three ways: it may be (1) endogenous, from increased absorption of iron; (2) exogenous, excess iron entering the body by way of multiple blood transfusions; or (3) due to nutritional disturbances, such as pellagra, which cause increased accumulation of iron in the tissues. The author describes 2 cases which illustrate the endogenous and exogenous mechanisms respectively.

Discussing the effect on the heart the author suggests that biochemical changes in enzyme systems and the destruction of phosphate-containing protein substances in the nuclei and sarcoplasm of cardiac muscle by the excess iron may be the cause of myocardial failure rather than any actual injury caused to the cardiac muscle cells by deposits of haemosiderin. Cases of myocardial haemosiderosis are extremely refractory to the ordinary treatment usually employed for congestive heart failure. It is suggested that repeated bleeding may remove some of the excess of iron and so prevent cardiac damage. *James W. Brown*

1305. **The Interplay of Coronary Vascular Resistance and Myocardial Compression in Regulating Coronary Flow**
C. J. WIGGERS. *Circulation Research* [*Circulat. Res.*] **2**, 271–279, May, 1954. 6 figs., 16 refs.

A study of the phasic flow curves derived from the coronary sinus in dogs indicates that venous blood from the areas of the heart supplied by both right and left coronary arteries drains into the coronary sinus. By comparing the coronary sinus flow during systole plus the period of isometric contraction with that during the rest of diastole it was found possible to assess the extent to which coronary flow is influenced by variations in the force of ventricular contraction and in coronary vascular resistance. The author's findings suggest that the main effect of ventricular compression is not to reduce coronary flow but to improve it, possibly by a massaging action.

[This paper is difficult to compress and should be read in full.] *C. Bruce Perry*

1306. **The Superior Vena Cava Syndrome.** (Vena cava superior syndromet)
A. H. ANDERSEN, A. T. HANSEN, E. HUSFELDT, A. PEDERSEN, and G. THOMSEN. *Ugeskrift for Læger* [*Ugeskr. Læg.*] **116**, 785–792, May 27, 1954. 6 figs., 32 refs.

The literature of superior vena caval occlusion is briefly reviewed, and it is noted that in the majority of cases the cause is a neoplasm, with aortic aneurysm taking second place. In a small number of cases the condition is due to thrombosis, and three such cases seen at Rigshospitalet, Copenhagen, are here reported in detail.

Two of the patients were men aged 39 and 49 years respectively, and the third was a 9-year-old girl. All 3 patients had had symptoms suggestive of superior vena caval obstruction for several years before being seen by the authors, when the classic signs were found, namely, cyanosis and oedema of the face and upper extremities, raised venous pressure in the jugular and forearm veins with normal pressure in the leg veins, and visible anastomotic veins on the anterior chest wall. The girl had in addition a considerable degree of hydrocephalus. Both the men had had a course of radiotherapy for supposed malignant lymphoma, the diagnosis of which had been based in one case on a mediastinal shadow detected radiographically, and in the other on a doubtfully positive result of lymph-node biopsy.

Angiocardiography was carried out in all cases, in one the solution being injected through a catheter the tip of which was lying in the axillary vein. The point of the obstruction and the collateral circulation were well outlined in each case. In one case the thrombosis involved the innominate and subclavian veins as well as the superior vena cava, so that operation was considered pointless. The other 2 patients were subjected to thoracotomy. In the case of the girl the thrombosed segment lay between the right atrium and the azygos vein, which

was grossly distended. At operation the latter was used as a shunt and implanted into the right auricle. In the case of the 39-year-old man the thrombosed segment involved the junction of the azygos vein with the superior vena cava and extended a short distance into both vessels; no attempt at a shunt was therefore undertaken. The mediastinal mass was seen to consist of vascularized, cartilaginous material; examination of an excised local lymph node revealed only non-specific inflammatory changes.

At follow-up examination 2 years later the girl had lost all signs and symptoms of superior vena caval obstruction, while the hydrocephalus had diminished. Both the men were still alive and their condition showed little change. *H. F. Reichenfeld*

CHRONIC VALVULAR DISEASE

1307. **The Clinical Diagnosis of Bicuspid Aortic Valve. A Study of Eighteen Cases**
J. TRANCHESI, R. CARRAL, I. DE AMORIM, and D. PEÑALOZA. *American Heart Journal* [*Amer. Heart J.*] **47**, 664–675, May, 1954. 6 figs., 17 refs.

The bicuspid aortic valve may be either congenital or acquired. The former type results from a failure of the two anterior cusps (which are derived from extensions of the septum of the truncus) to separate or from a failure of the posterior cusp (which arises from the dorsal swelling of the truncus arteriosus) to develop. In the acquired type fusion of the valve leaflets results from an inflammatory process, which is usually rheumatic in origin. Out of a total of 1,152 patients with cardiovascular diseases examined post mortem at the National Cardiological Institute of Mexico, 11 cases of congenital and 7 of acquired bicuspid aortic valve were found. In 8 of the congenital cases subacute bacterial endocarditis was also present.

It is impossible to diagnose the acquired type of bicuspid aortic valve on clinical grounds, nor would it appear to be of any importance to do so. The congenital type, however, should be suspected when a patient with a previously normal heart develops subacute bacterial endocarditis with aortic incompetence. [This, of course, was pointed out by Lewis and Grant many years ago.] *C. W. C. Bain*

1308. **A New Operation for Mitral Regurgitation**
J. HAYWARD. *Australian and New Zealand Journal of Surgery* [*Aust. N.Z. J. Surg.*] **23**, 257–267, May, 1954. 6 figs., 1 ref.

The author describes a new operation which he has devised at the Royal Melbourne Hospital for the treatment of mitral regurgitation. Full details of the technique are given. In discussing the pathology of mitral disease he states that in all cases there is an element of regurgitation. [This is not the generally accepted view.] He maintains that there are two major types of mitral incompetence: those in which the disease has virtually destroyed the postero-lateral cusp, leaving the anterior one mobile; and those in which the disease is more widespread, with gross contraction of the valves and the chordae tendineae.

In order to block the gap left by the shrunken posterior cusp he has invaginated the atrial appendage and sewn it across the mitral orifice in 2 cases, both of which are fully reported. He also suggests a modification of this technique which, he considers, might be applicable to patients who have "funnel" valves. In the 2 patients treated by this method there was a marked improvement for a short time, but it is stated in an addendum to the paper that both of them are now back to their preoperative condition. *J. R. Belcher*

1309. **The Clinicopathologic Correlation of Lung Biopsies in Mitral Stenosis**
E. M. GOYETTE, C. J. FARINACCI, J. H. FORSEE, and H. A. BLAKE. *American Heart Journal* [*Amer. Heart J.*] **47**, 645–652, May, 1954. 8 figs., 8 refs.

In long-standing mitral stenosis changes in the pulmonary vessels are known to produce additional obstruction to the flow of blood. At the Fitzsimons Army Hospital, Denver, Colorado, the authors attempted to correlate the findings on clinical examination and cardiac catheterization with the pathological changes observed in lung-biopsy specimens in cases of mitral stenosis. Tissue from the lingula was obtained from 15 patients at the time of mitral valvotomy and examined histologically, necropsy material from 10 patients without cardiac or pulmonary disease being examined at the same time. Clinical factors assessed included the age of the patient, duration and severity of symptoms, *x*-ray appearance of the lung fields, changes in the electrocardiogram, and findings on catheterization. The alveolar changes ranged from capillary congestion to fibrosis and emphysema. The vascular changes consisted of intimal fibrosis and medial hypertrophy and scarring. Arteritis was not observed.

The small number of patients and the short follow-up period permitted a clinical impression only—namely, that patients with far-advanced pulmonary vascular changes do not benefit as much from mitral valvotomy as do patients without this complication, but that there are notable exceptions. *E. G. Rees*

1310. **Studies on the Renal Circulation and Renal Function in Mitral Valvular Disease. I. Effect of Exercise**
L. WERKÖ, E. VARNAUSKAS, H. ELIASCH, J. EK, H. BUCHT, B. THOMASSON, and J. BERGSTRÖM. *Circulation* [*Circulation (N.Y.)*] **9**, 687–699, May, 1954. 6 figs., 36 refs.

In this study of renal function in mitral valvular disease, carried out at St. Erik's Hospital, Stockholm, the authors first measured, by means of cardiac catheterization, the right atrial and pulmonary vascular pressures and the cardiac output in the resting state in 72 cases of mitral stenosis. Inulin and *p*-aminohippurate (PAH) clearances and urinary sodium excretion were determined simultaneously. These observations were repeated on 31 of the patients after light steady exercise, performed for about 15 minutes. In 2 cases the right renal vein was catheterized and PAH extraction determined. The patients were divided into three groups

according to degree of disability, those with raised right atrial pressure being placed in a separate sub-group.

It was found that the cardiac output was reduced and pulmonary vascular pressure raised in rough proportion to the severity of disability. Clearance of PAH at rest was also reduced in rough proportion to the degree of alteration in the circulatory measurements; inulin clearance at rest was likewise decreased, but to a much less extent. The few patients with raised right atrial pressure showed similar results.

In the patients with normal right atrial pressure at rest exercise produced an increase in cardiac output, pulmonary vascular pressure, and renal vascular resistance, and a reduction in PAH clearance and sodium excretion, but right auricular pressure and inulin clearance were unaltered. In the patients with raised right atrial pressure at rest exercise produced a further rise in right atrial pressure; pulmonary vascular pressure increased, but cardiac output remained unchanged, while there was little change in PAH and inulin clearance and in renal vascular resistance.

The authors conclude that in patients with mitral stenosis at rest the changes in renal function are similar to those seen in normal individuals during heavy exercise. During light exercise, which would be insufficient to produce measurable change in normal individuals, there is a further depression of renal function in patients with mitral stenosis. The absence of a fall in PAH clearance during exercise in the patients with raised right atrial pressure suggests that in these cases the renal blood flow is already at the lowest possible level.

Albert Venner

1311. **Studies on the Renal Circulation and Renal Function in Mitral Valvular Disease. II. Effect of Apresoline** L. WERKÖ, E. VARNAUSKAS, J. EK, H. BUCHT, B. THOMASSON, J. BERGSTRÖM, and H. ELIASCH. *Circulation* [*Circulation (N.Y.)*] **9**, 700–705, May, 1954. 3 figs., 18 refs.

In the second part of this study [see Abstract 1310] the authors observed the effect of " apresoline " (hydrallazine) on the renal function of 11 patients with mitral stenosis. The drug was given during cardiac catheterization by intravenous drip at the rate of 0·3 to 0·5 mg. per minute for about 30 minutes, noradrenaline being given simultaneously at the rate of 0·006 mg. per minute intravenously to counteract the hypotensive effect of the hydrallazine.

The immediate effect of this infusion was to cause an increase in systemic blood pressure and a decrease in renal blood flow, these changes being due to the noradrenaline. After 15 minutes the effect of the hydrallazine became predominant and systemic blood pressure fell, usually to a little below the resting level, while renal blood flow increased to a mean value for the group of nearly double the resting value, while in individual cases it increased to several times the resting level. When exercise was performed during the administration of hydrallazine cardiac output increased while renal blood flow also increased or remained the same, from which it appears that the action of the drug is to counteract the effect which physical effort usually has on renal function in mitral stenosis. Hydrallazine has been shown to produce an increase in renal blood flow in normal and in hypertensive subjects. The fact that noradrenaline suppresses the effect of hydrallazine on the systemic blood pressure without altering its effect on renal blood flow suggests that these two actions are mediated by independent mechanisms.

Renal venous catheterization in two cases showed that PAH extraction during the administration of hydrallazine fell from 90 to 80%. Sodium excretion showed large variations; when the arterial blood pressure remained constant sodium excretion showed changes similar to PAH clearance, but when there was a severe fall in blood pressure sodium excretion was considerably reduced. The authors conclude that the effect of hydrallazine in mitral stenosis suggests that the decrease of PAH clearance (and presumably, therefore, of renal blood flow) in this condition is functional and reversible.

Albert Venner

DISTURBANCES OF RHYTHM AND CONDUCTION

1312. **Quinidine in the Treatment of Auricular Fibrillation** O. BEDARD. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 530–534, May, 1954. 9 refs.

The value of quinidine in the treatment of auricular fibrillation has been known since 1918, but only in the last 10 years has its action been extensively studied. The early reports on this drug perhaps overemphasized its dangers, and in the author's opinion the danger from auricular fibrillation, which frequently causes heart failure and is always a potential source of embolism, is greater than the danger from quinidine. Also, reversion to a normal sinus rhythm following the administration of quinidine increases cardiac output and diminishes the frequency of embolism.

In this report from Ottawa General Hospital (University of Ottawa) the author discusses 67 cases of auricular fibrillation in 39 of which the condition was due to arteriosclerotic disease, in 7 to hypertensive disease, and in 21 to rheumatic heart disease; the patients' ages ranged from 26 to 84 years. In 60 (89%) of the 67 cases quinidine brought about reversion to normal sinus rhythm. The drug was administered according to a definite schedule as follows. A test dose of 0·2 g. was given the first day, and if there was no untoward reaction the same dose was repeated 3 times on the second day and 6 times on the third day. If reversion to normal rhythm was not obtained the course was repeated, each dose being increased by 0·1 g. on successive days so that by the eleventh day the patient might be taking 6 doses of 1 g. each daily. Throughout treatment electrocardiograms were taken to detect toxicity, and evidence of conduction defects was considered to be a contraindication to any further increase in the dose. When reversion to normal rhythm occurred the dose necessary for this reversion was continued for 24 hours and then gradually reduced until an arbitrary maintenance dose of 0·2 g. 3 times a day was reached. A maintenance dose of 0·1 g. of digitalis leaf was given throughout treatment, except when the pulse rate was

below 60 or the P–R interval was increased on the electrocardiogram.

Side-effects of the drug, mainly gastrointestinal and nervous, were in most cases mild, and in only 6 had treatment with quinidine to be withdrawn. Seven of the patients died during treatment, and in 3 of these cases it is possible that death may have been precipitated by the drug. It is claimed, however, that fear of quinidine is unreasonable, and that by its use correction of auricular fibrillation in patients with treated heart failure is a practical and often desirable procedure.

James W. Brown

1313. **The Effect of Chronic Auricular Fibrillation on the Operative Risk**

J. A. FINKBEINER, F. WROBLEWSKI, and J. S. LADUE. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 535–543, May, 1954. 47 refs.

The authors discuss the effect of chronic auricular fibrillation on the operative risk, as observed at the Memorial Center for Cancer and Allied Diseases, New York, in 60 patients with cardiovascular disease and auricular fibrillation who underwent 76 major surgical operations of at least one hour's duration, mainly for neoplastic disease, with an operative mortality of 5%. In 54 (71%) of the operations changes occurred in the pulse or blood pressure which were classified as mild (34 cases), moderate (16 cases), or severe (4 cases) according to their degree or duration. In the postoperative period there were cardio-pulmonary complications in 17 cases, resulting in postoperative death in 3, while 15 of the 60 patients died of cardiovascular disease within 39 months.

Preoperative preparation was considered to be important, and inadequate digitalization, a history of recent congestive heart failure, angina pectoris, and poor cardiac function were found to be associated with an increase in the complication rate. The authors conclude that a patient with chronic auricular fibrillation probably runs no greater operative risk than a patient with equal cardiac damage but no fibrillation, provided that adequate preoperative preparation is assured. This is especially important in relation to digitalization of the elderly " slow fibrillators ", whose slow pulse does not necessarily indicate full therapeutic saturation with the drug. The authors employ an atropine test and a standard exercise test to determine the completeness of digitalization.

James W. Brown

1314. **Methoxamine Hydrochloride in the Treatment of Paroxysmal Supraventricular Tachycardia. Report of Three Cases**

L. A. CHOTKOWSKI, C. P. POWELL, and R. L. RACKLIFFE. *New England Journal of Medicine* [*New Engl. J. Med.*] 250, 674–676, April 22, 1954. 4 figs., 6 refs.

The treatment at New Britain (Connecticut) General Hospital of attacks of paroxysmal supraventricular tachycardia in 6 patients by the intravenous injection of 5 to 20 mg. of methoxamine (" vasoxyl ") is reported. Continuous electrocardiography demonstrated the termination of the arrhythmia within a matter of seconds in each case. This was preceded by one or more ventricular extrasystoles, but no prolonged period of asystole was experienced, while after normal rhythm had been established no further extrasystoles were noted. This would seem to indicate that this drug, unlike some of the other pressor amines, does not produce cardiac irritability.

T. Semple

1315. **Treatment of Stokes–Adams Disease by External Electric Stimulation of the Heart**

P. M. ZOLL, A. J. LINENTHAL, and L. R. NORMAN. *Circulation* [*Circulation (N.Y.)*] **9**, 482–493, April, 1954. 4 figs., 7 refs.

The authors, working at Harvard Medical School and Beth Israel Hospital, Boston, report the results of their use of an electrical stimulator (briefly described) placed over the praecordium in 14 cases of Stokes–Adams disease. The stimulus from the artificial pacemaker could be varied in strength and frequency, and was designed to overcome periods of extreme ventricular bradycardia or standstill in cases of complete auriculo-ventricular block. Electrocardiograms demonstrated the effectiveness of this external electrical stimulator in 13 of the 14 patients. Stimulation was effective during periods of sinus rhythm, nodal rhythm, and partial and complete A-V block. Detailed cardiac histories are given of the 14 patients, of whom 10 eventually died, 8 from a Stokes–Adams attack.

Syncope due to ventricular standstill was terminated immediately. An effective circulation was maintained for periods of up to 4 days with continuous stimulation. In most cases idioventricular rhythm returned after withdrawal of the artificial stimulation, and one patient has had no further syncopal attacks for a year. The stimulator proved ineffective in ending attacks of persistent ventricular tachycardia, which proved fatal in 3 cases; it did, however, prevent the recurrence of such attacks during its application for ventricular standstill. No untoward cardiac effects were observed during the external stimulation, and the chest pain and muscular twitching which occurred in some cases were minimized by the use of pethidine hydrochloride and paraldehyde. The authors conclude that the use of such a stimulator can be recommended for abrupt circulatory arrest from any cause.

D. W. Barritt

CORONARY DISEASE AND MYOCARDIAL INFARCTION

1316. **The Risk of Major Surgery in Patients with Coronary Artery Disease**

R. P. LOCHHEAD, C. S. COAKLEY, and J. M. EVANS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 624–627, June, 1954. 5 refs.

The morbidity and mortality observations are reviewed in 32 subjects with coronary artery disease undergoing 51 major operative procedures during the years 1950 to 1952. There were 3 deaths and one postoperative complication in 17 patients with myocardial infarction undergoing 30 operations; in 15 patients with angina pectoris

undergoing 21 operations there were no deaths and 2 postoperative complications. There were no operative complications in either group of patients. These figures compare favorably with others recently reported and reflect the improved outlook for the patient with coronary artery disease undergoing surgery.—[Authors' summary.]

1317. **The Incidence of the Thromboembolic Phenomena Associated with the Treatment of Acute Coronary Artery Occlusion**

R. W. KISSANE, R. S. FIDLER, and J. J. CONN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 663–671, June, 1954. 10 refs.

1318. **Angina of Effort. Use of Heparin for its Control**

F. H. STEVENSON and D. G. WILSON. *Lancet* [*Lancet*] **1**, 1319–1320, June 26, 1954. 10 refs.

The value of heparin in the relief of anginal pain is discussed with reference to the results obtained in 22 patients by a group of general practitioners in the area of Bushey and District Hospital, Herts. Only those patients were included whose daily requirement of glyceryl trinitrate and whose exercise tolerance were known. An intramuscular injection of 100 mg. of heparin was given to these patients twice a week for 4 weeks. This was followed by an intramuscular injection of saline twice a week for 3 weeks, and then by an injection of 100 mg. of heparin twice a week for a further 5 weeks.

In 4 cases there was marked improvement, the pain being less frequent and severe. Improvement was noted in 6 patients who had taken special care to avoid pain, "doubtful improvement" in 5, and no change in 4. The remaining 3 patients became worse, one developing an infarct during treatment. Only one of the 10 patients who improved noticed any difference when saline was substituted for heparin. There was no consistent effect on the blood cholesterol level, which was estimated before and after treatment, and the electrocardiogram was unchanged.

[In a letter to the *Lancet* (1954, **1**, 1187) Davies and Barritt refer to a similar investigation.]

D. W. Barritt

1319. **Trials of Methylchromone in the Basic Treatment of Angina Pectoris.** (Essais d'utilisation de la méthyl-3-chromone comme traitement de fond de l'angine de poitrine)

P. SOULIÉ, P. CHICHE, J. CARLOTTI, and J. BAILLET. *Presse médicale* [*Presse méd.*] **62**, 847–849, June 2, 1954. 5 figs., 34 refs.

3-Methylchromone, which has been synthesized and studied because of its chemical relationship to khellin, has been shown experimentally to exert, like the latter, a direct dilator action on the perfused coronary arteries. The present authors also showed that 3-methylchromone diminishes the tone of the isolated duodenum of the rat, but does not affect contractions induced by acetylcholine. Toxicity studies in the rat revealed that a daily oral dose of 0·66 g. per kg. body weight was fatal to 3 of 10 rats, while lower doses caused no demonstrable effects except some somnolence.

In a clinical trial carried out by the authors, 45 outpatients suffering from angina of effort due to coronary arterial disease were given 3-methylchromone in doses of 0·1 g. three or four times daily by mouth for 10 days. The period of administration of the drug was preceded by a 10-day period during which the patients received inert but indistinguishable tablets. At the end of each 10-day period the patients were interviewed, the criteria of improvement being diminution in the frequency and severity of the anginal attacks and increased tolerance of effort. Ten (22%) of the patients reported improvement after taking the placebo and 22 (49%) after 3-methylchromone. Some degree of somnolence was experienced by all patients taking the drug, but no other side-effects were noted. Many of the patients who reported benefit from 3-methylchromone were then given a second course of the placebo, and in no case was the previous improvement maintained. The best results were obtained in cases in which the electrocardiogram was normal at rest and showed no depression of the ST segment after exercise. The authors believe that the presence of ST depression indicates coronary insufficiency so severe that it is unlikely that any dilator drug could confer symptomatic benefit. *Bernard Isaacs*

1320. **Acute Myocardial Infarction Treated by the Chair Rest Regimen. Thirty Consecutive Cases Managed by the Levine Armchair Method**

J. L. WILSON and J. H. WARD. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 226–230, May 15, 1954. 18 refs.

The authors report the results obtained with a chair-rest regimen in the management of 30 consecutive proved cases of myocardial infarction at the United States Naval Hospital, Bremerton, Washington. The patient was lifted into a large, comfortable, upholstered chair by the bedside as soon as shock had passed and the presence of complications had been excluded. The majority of the patients tolerated 3 to 6 hours in the chair on the first day and at least 10 hours on the third or fourth day. Other treatment included administration of anti-coagulants, support for the lower limbs by application of an elastic bandage or, preferably, elastic stockings, and administration of oxygen, liberally in the first 48 hours and then as a routine for one hour after each meal during the first week. At night the head of the bed was raised to avoid hypostatic congestion of the lungs. The patient was assisted to a bedside commode, thus avoiding the exertion necessary in using a bed-pan. After 21 days walking was allowed, activity being gradually increased during the next 14 days. On the average the patient was up in a chair on the 5th day, seated all day by the 8th day, ambulant by the 24th, and discharged on the 33rd day.

Of the 30 patients, 3 died—one from massive infarction involving the posterior and lateral aspects of the heart, one from rupture of the left ventricle, and one from perforated peptic ulcer and peritonitis in addition to acute myocardial infarction.

The authors claim that with this method of treatment the mortality is "uncommonly low" and the morale

of the patients is high. They discuss the dangers of long periods of recumbency and the physiological changes which result. [No control series is described.]

H. G. Farquhar

HEART FAILURE

1321. **The Effect of Ganglion Blocking Agents in Congestive Heart Failure**

C. R. SHUMAN, N. LEARNER, and J. H. DOANE. *American Heart Journal* [*Amer. Heart J.*] **47**, 737–744, May, 1954. 2 figs., 15 refs.

In this paper from the Temple University Hospital, Philadelphia, are reported the results obtained with two autonomic ganglion blocking agents in congestive heart failure due to various causes, including rheumatic mitral stenosis, hypertension, arteriosclerosis, and scoliosis. A total of 21 patients received an intravenous injection of either 150 to 500 mg. of tetraethylammonium bromide or 12·5 to 50 mg. of hexamethonium iodide. It was found that the venous pressure fell simultaneously with the arterial pressure, while the vital capacity increased, resulting in significant clinical improvement, with reduction in dyspnoea and orthopnoea. This improvement lasted one to several days and was more marked in patients with milder degrees of congestive failure. The results of estimation of the digital blood flow and skin temperature were variable, but the usual increase in cutaneous flow noted in patients without heart failure was not observed in most of the patients in this series, suggesting that other vascular areas, such as the visceral or muscle vessels, had been opened up by the release of vasoconstrictor reflexes. Thus, release of neurogenic reflexes increasing arteriolar and venular tone reduced the work of the left ventricle, and lowered the elevated venous filling pressure of the right heart. The authors consider autonomic blockade to be of value in the treatment of pulmonary congestion. *I. Ansell*

1322. **Potassium Deficiency in Congestive Heart-failure. Three Cases with Hyponatraemia, Including Results of Potassium Replacement in One Case**

J. H. CORT and H. L. MATTHEWS. *Lancet* [*Lancet*] 1, 1202–1206, June 12, 1954. 1 fig., 13 refs.

The occurrence of hyponatraemia and hypochloraemia in patients with chronic cardiac failure after prolonged treatment with mercurial diuretics has been reported by Squires *et al.* (*Circulation*, 1951, **4**, 679, 697, and 868; *Abstracts of World Medicine*, 1952, **11**, 159, 160, and 263). In this paper from the Queen Elizabeth Hospital and the General Hospital, Birmingham, the authors describe observations on 3 patients with chronic cardiac failure associated with a low serum sodium concentration and resistance to mercurial diuretics. Electrolyte balance studies were carried out on 4 successive days after the patients had been on a constant diet for 3 days, and muscle biopsy was performed for the determination of tissue electrolyte content. Case histories and detailed results of the investigations are given and discussed. The patients were in consistent daily negative potassium balance and positive sodium balance. The muscle tissue analysis revealed a large deficit of intracellular potassium and the presence of cellular oedema.

Two of the patients died, but the third was treated with a high potassium intake without mercurials, while digitalization was maintained. During this treatment balance studies were continued and a second muscle biopsy was performed 50 days after the first. As soon as potassium was given, as a dose of 9 g. of potassium citrate daily, the patient showed a positive potassium balance. As after one week there were no signs of potassium intoxication the dose of potassium was increased at intervals, and on each occasion the positive potassium balance increased correspondingly. Meanwhile the serum sodium level also rose and the patient improved clinically, with diminution of both oedema and cyanosis. Eventually, on a daily potassium intake of 200 mEq., normal tissue and serum potassium levels were attained, the positive potassium and sodium balances fell, and sodium was excreted in the urine.

The authors stress that potassium replacement therapy must be started with small doses for fear of potassium intoxication, and that special care must be taken in cases complicated by renal failure. *D. Goldman*

1323. **Acetyl-digitoxin. Clinical Observations on the Treatment of Patients with Advanced Congestive Heart Failure**

W. LÖFFLER, A. F. ESSELLIER, and G. FORSTER. *American Heart Journal* [*Amer. Heart J.*] **47**, 898–911, June, 1954. 4 figs., 21 refs.

Digitoxin and other pure glycosides have the advantages that their effects are constant and the dose can be assessed gravimetrically, but they suffer from the disadvantage that they cause frequent and persistent side-effects owing to cumulation. In an attempt to produce a drug with a greater therapeutic margin acetyl-digitoxin was prepared from lanatoside A, and pharmacological experimentation has shown it to be well absorbed from the intestine, to be capable of reducing the heart rate, and to be less toxic than digitoxin. It was therefore tried out at the University Hospital, Zürich, over a period of 18 months in the treatment of 120 patients with advanced congestive heart failure. Two-thirds of the patients were over 60 years of age, and three-quarters of them had one of several complications, including thrombosis, pulmonary infection, pneumonia, apoplexy, or cirrhosis of the liver.

It was found that the rate of intestinal absorption of this drug was 67%, as compared with 80% for digitoxin. It acts within 20 to 30 minutes of intravenous injection and within 2 to 4 hours when given orally, while its effect lasts about 9 days and its rate of elimination is 14%. It reduces the heart rate, increases cardiac efficiency, and has an excellent diuretic effect. Side-effects were noted in one-quarter of the patients during the initial or maintenance stages of treatment, but these did not differ from those produced by other digitalis glycosides; they consisted in nausea and vomiting, visual disturbances (in 2 cases), and an acute psychosis with delirium in one patient. Side-effects were less frequently observed later in the trial when the dosage was reduced. A fixed dosage

scheme was considered to be as impracticable as with other glycosides, and dosage has to be adjusted to suit the individual patient. The high rate of fixation of the drug makes it generally very suitable for prolonged treatment of patients with chronic heart failure. Also, as its effect is more quickly reversible than that of digitoxin, treatment with acetyl-digitoxin can be more easily controlled. Of the 120 cases treated, good or excellent results were obtained in 43% and fair results in 38%, the remaining 19% of cases proving resistant to this and other types of therapy. *Robert Hodgkinson*

HYPERTENSION

1324. **Hypertension and " Venous " Leg Ulcers**
S. T. ANNING. *Lancet* [*Lancet*] **1**, 1271–1272, June 19, 1954. 8 refs.

An investigation was carried out at the General Infirmary at Leeds to determine whether the mean arterial blood pressure in patients with post-thrombotic or varicose ulcer of the leg is within the normal range. The arterial blood pressure in 696 women aged 20 to 94 and in 316 men aged 20 to 84, all of whom had ulceration of the leg from defective venous circulation, was determined and compared with that of a sample of the general population. It was found that the blood pressure of the women between the ages of 35 and 74 was significantly higher than that of the controls in the same age group. The number of men observed was not sufficiently large for conclusions to be drawn.

The cause of this association is obscure. In the present series there was no evidence that body weight was a factor. The author states that while the opening up of arteriovenous shunts after deep venous thrombosis may be of significance in relation to hypertension, there is no reason to suppose that these shunts result in hypertension. It is possible that hypertension is a coincidental finding, but that it predisposes to ulceration in patients with venous congestion of the lower limbs. *Peter Martin*

1325. **Intravenous Hexamethonium Sensitivity and Responses to Oral Treatment**
D. M. GREEN and E. J. ELLIS. *Circulation* [*Circulation (N.Y.)*] **9**, 521–526, April, 1954. 5 figs., 6 refs.

In an effort to distinguish if possible between neurogenic and humoral factors in hypertension and to determine whether the response to the intravenous injection of hexamethonium would provide any indication of the likely response to oral therapy the authors carried out an investigation on 23 cases of essential hypertension under treatment at Los Angeles County General Hospital. The patients' ages ranged from 26 to 72 years, and none of them had evidence of coronary artery disease or heart failure. Blood pressures were determined by sphygmomanometry with the patient in the sitting position. A 2% solution of hexamethonium chloride was injected intravenously in increments of 1 to 10 mg., depending upon the response of the blood pressure, and the amount of the drug required to produce a fall of the systolic pressure halfway to normal was used as the index of hexamethonium sensitivity. In addition, 21 of the patients were given hexamethonium by mouth for periods up to 6 months, the lowest blood pressure reached during this period being taken as a measure of sensitivity to oral therapy.

In every case the blood pressure was reduced to the desired level by intravenous hexamethonium, but the dose required to achieve this varied from 1·4 to 23·0 mg. per square metre of body surface. The cases were therefore divided into " sensitive " and " resistant " groups according to dose, the critical dose taken as the dividing line being 4 mg. per sq. m. body surface. No difference could be found between the two groups in respect of original blood pressure, pulse rate, heart size, retinal changes, or known duration of hypertension; the sensitive group had a slightly greater average age. Those patients most sensitive to intravenous hexamethonium were also most sensitive to oral therapy. The authors conclude that (1) no part of the vasoconstrictive mechanism in essential hypertension is not under autonomic control, and (2) response to intravenous hexamethonium is a reliable guide to the response to oral therapy.
D. W. Barritt

1326. **Effects of Withdrawal and Restoration of Dietary Sodium Chloride upon Urinary Electrolytes in Patients with Hypertension**
F. T. HATCH. *Metabolism* [*Metabolism*] **3**, 160–167, March, 1954. 7 refs.

At the Goldwater Memorial Hospital, New York, 11 patients with severe hypertension (blood pressure at least 200/120 mm. Hg), half of whom had some degree of heart failure, were transferred abruptly from a diet containing 40 mEq. of sodium, 100 mEq. of chloride, and 80 mEq. of potassium per day to a Kempner rice diet containing approximately 4 mEq. of sodium and 10 mEq. of chloride per day, the potassium intake being little changed. The serum concentration and the total urinary excretion of these ions were measured, the period on the very low salt intake lasting 5 weeks. The same observations continuing, 8·5 mEq. (0·5 g.) or 17 mEq. (1 g.) of sodium chloride was then added as an addition to the Kempner diet of 4 of the patients.

During the Kempner regimen there was a gradual fall in urinary sodium and chloride excretion over a period of about 3 weeks. The total body content of sodium decreased by amounts varying from 30 to 480 mEq. and that of chloride by 70 to 620 mEq. Although 4 patients showed no appreciable decline in basal blood pressure, there was an average decrease in pressure for the whole group of 22 mm. Hg systolic and 12 mm. Hg diastolic. When the sodium chloride was added to the rice diet there was a rapid increase of chloride ion in the urine, but practically none of the sodium appeared in the urine for at least 4 weeks. No cause for this dissociation was found. *G. A. Smart*

1327. **Development of Hypertensive Manifestations after the Disappearance of Hypertension**
G. A. PERERA. *Circulation* [*Circulation (N.Y.)*] **10**, 28–29, July, 1954. 1 ref.

Haematology

1328. **Serum and Urine Concentrations of Vitamin B_{12} following Oral Administration of the Vitamin**
W. R. PITNEY and M. F. BEARD. *Journal of Clinical Nutrition* [*J. clin. Nutr.*] **2**, 89–96, March–April, 1954. 22 refs.

From the U.S. Army Medical Nutrition Laboratory, Denver, Colorado, the authors report a study of the levels of vitamin B_{12} (cyanocobalamin) in the serum and urine following oral administration of the vitamin both to normal subjects and to patients with pernicious anaemia. Vitamin concentration was measured microbiologically, *Euglena gracilis* being used as the test organism.

In 56 normal subjects the serum cyanocobalamin level ranged from 86 to 460 $\mu\mu$g. per ml., with a mean figure of 212 $\mu\mu$g. per ml.; in only 4 of these subjects was a small amount of free vitamin present. The maximum figure observed in 13 patients with pernicious anaemia was only 44 $\mu\mu$g. per ml. and in 8 cases the serum contained no cyanocobalamin at all. In both normal subjects and anaemic patients in relapse the oral administration of 1,000 μg. of cyanocobalamin had no effect on the serum level. If the dose was increased to 5,000 μg., however, the serum concentration of the vitamin increased in both groups, but the excretion of cyanocobalamin in the urine in both controls and patients following such massive oral doses was negligible. The authors conclude that the absence of urinary excretion of the vitamin is due to the fact that cyanocobalamin given orally is only slowly absorbed from the intestine and can thus be bound by serum protein, being present in the blood only in the bound form. When, however, it is given by parenteral injection the circulation is flooded with the free vitamin and some is excreted by the kidney before becoming bound. *Janet Vaughan*

1329. **The Association of Hemolytic Anemia with Sarcoidosis**
A. E. DAVIS, J. P. BELBER, and E. R. MOVITT. *Blood* [*Blood*] **9**, 379–383, April, 1954. 3 figs., 11 refs.

1330. **Giant Follicle Hyperplasia: a Study of its Incidence, Histopathologic Variability, and the Frequency of Sarcoma and Secondary Hypersplenic Complications**
T. S. EVANS and C. A. DOAN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **40**, 851–880, May, 1954. 12 figs., bibliography.

In this paper from Yale and Ohio State Universities the authors present a critical review of the literature on giant follicle hyperplasia together with a report on 16 personally studied cases. Splenomegaly occurred in 11 of the 16 cases and in 8 of them splenectomy was performed for more or less acute cytopenic episodes; full clinical histories of these 8 patients are given. The authors note that in giant follicle lymphoma splenic involvement occurs early in the disease and is relatively common, being much more frequent than involvement of the bone marrow; the course is usually a chronic one. The combination of early splenomegaly and the chronic nature of the disease renders these patients peculiarly susceptible to the development of secondary hypersplenism, 3 of the 8 patients having haemolytic anaemia, 2 having thrombocytopenic purpura one having neutropenia and thrombocytopenia, and 2 having peripheral pancytopenia. In all 8 cases the syndrome was reversed by splenectomy. One of the patients with pancytopenia developed lymphosarcoma 7 years after splenectomy and died; one had developed reticulum-cell sarcoma 9 years after the operation, but had responded to treatment and was still alive 10 months after the beginning of treatment. Of the 8 patients without the hypersplenic syndrome, 3 had splenomegaly and 2 of these had anaemia. Of this whole group, 3 patients developed sarcoma and died, but of the other 5, one is alive 14 years and one 5 years after the original diagnosis, while the other 3 have survived for periods of 18 months to 4 years.

After a critical review of the literature [extending only up to 1950] an analysis of 104 cases there recorded is given. From their own observations and those in the literature the authors reach the following conclusions. (1) Giant follicle hyperplasia is a relatively benign condition primarily due to reticulo-endothelial cell hyperplasia. (2) The actual cytological detail varies from case to case and even in the same case at different times, the cells within the hyperplastic follicles appearing as a mixture of large, non-phagocytic, reticulum cells, or as free mononuclear phagocytes, or as lymphoblasts. (3) When the spleen is involved, hypersequestration of one or more of the blood cell types occurs, and the bone marrow responds to this by increased production of the cell type affected. Splenectomy brings about the prompt return of a normal blood picture. (4) If the cytopenia recurs after splenectomy, the presence of a hypertrophied accessory spleen should be suspected. (5) The benign type of the syndrome is relatively easily controlled by *x* irradiation or treatment with radioactive phosphorus and the prognosis is reasonably good unless sarcomatous changes develop. (6) The aetiology of the disease is not known; the authors suggest that it may be a " reversible or controllable physiologic functional response rather than always a progressive, irreversible pathologic-malignant mutation of the cells in the enlarged germinal centres ".

[This paper was presented in part at the International Haematology Congress at Cambridge in 1950, and the delay in its publication has meant that most of its contents are now familiar. Among more up-to-date accounts which have appeared since 1950 is that by Wetherley-Mein *et al.* (*Quart. J. Med.*, 1952, **21**, 327; *Abstracts of World Medicine*, 1953, **13**, 129).] *M. C. G. Israëls*

Respiratory System

1331. **Needle Biopsy of the Lung**

F. R. DUTRA and C. L. GERACI. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 21–24, May 1, 1954. 4 figs., 8 refs.

Writing from the Veterans Administration Hospital, San Francisco, the authors describe 3 cases in which examination of lung tissue obtained by needle biopsy proved helpful in establishing the nature of a radiological opacity. The Vim–Silverman biopsy needle as described by Tripoli and Holland (*South med. J.*, 1940, **33**, 559) was used for the purpose and found to be satisfactory. In all 3 cases the diagnosis of neoplasm was established by biopsy examination, the presence of carcinoma cells being demonstrated in the specimen. The biopsy needle is inserted into the suspected area under fluoroscopic screen control; as the needle is rather short only masses near the periphery, and therefore in comparatively safe areas, can be reached. There were no untoward incidents during biopsy in the 3 cases described. The authors point out, however, the possible dangers of the method, which include the production of haemothorax, empyema, or pneumothorax, or the implantation of tumour cells in the needle track; this last mishap occurred in one of the authors' patients.

In discussing the limitations of the method the authors express the view that it should be used mainly to confirm the diagnosis when other diagnostic methods have failed, and be limited to inoperable cases as a preliminary to palliative treatment such as irradiation or chemotherapy. If the mass is due to a tuberculous or other inflammatory process thoracotomy and resection is the procedure of choice. *I. McLean Baird*

1332. **Movements of the Thoracic Cage and Diaphragm in Respiration**

O. L. WADE. *Journal of Physiology* [*J. Physiol.* (*Lond.*)] **124**, 193–212, May 28, 1954. 12 figs., 14 refs.

Further to a previous, similar study with Gilson (*Thorax*, 1951, **6**, 103; *Abstracts of World Medicine*, 1951, **10**, 452) the author has now investigated, at the Medical Research Council Pneumoconiosis Research Centre, Cardiff, the relationship between movements of the diaphragm and changes in the circumference of the chest during respiration, and also the question of independent movements of the diaphragm and chest wall and whether these are under voluntary control. The method employed was similar to that in the earlier study. While a spirograph recorded pulmonary ventilation, diaphragmatic movements were tracked by *x*-ray screening. Corrections were made for geometric distortion and for changes in diaphragm level caused by vertical movement of the thorax. Chest expansion was measured by a modification of Whitney's method (*J. Physiol.* (*Lond.*), 1949, **109**, 5) for measuring changes in limb volume. A transducer of mercury-filled rubber tubes was wrapped round the chest; stretching the tubes on inspiration lengthens and narrows the mercury column, so increasing its electrical resistance, which can be measured. Details of the design, calibration, and performance of the transducer are given.

In all, 10 healthy male subjects aged 24 to 36 years were studied. In quiet respiration the tidal diaphragmatic movement averaged 1·5 cm. and the tidal change in chest circumference was about 1·2 cm. in the erect position and 6·7 cm. in the supine. During deep breathing the total diaphragmatic excursion was 7 to 13 cm. and the change in chest circumference 5 to 11 cm. From his calculations the author postulates that in achieving full vital capacity about one-quarter of lung ventilation is due to chest expansion and the remainder to diaphragmatic movement.

In the tests of voluntary control of the type of breathing 4 trained subjects attempted to perform either predominantly " thoracic " or " diaphragmatic " breathing; the diaphragm movement relative to the thoracic cage was found to remain unchanged. In " costal " breathing, the thorax is elevated during inspiration and the abdominal wall retracted, whereas in diaphragmatic breathing the anterior abdominal wall is protracted. No evidence of voluntary control of the diaphragm was found, although some subjects seemed to be able to inhibit changes of chest circumference. Diaphragmatic and chest movements were closely coordinated except during voluntary hyperventilation. Elevation of the thorax occurred in some subjects, mainly at the end of deep inspiration when the subject was erect, and was most marked in hyperventilation. It is probably due to extension of the spine and, while itself contributing little to lung ventilation, it may aid the rapid and large movements of the diaphragm which occur in hyperventilation. *D. Goldman*

1333. **The Arterial Oxygen and Carbon Dioxide Tension during the Postoperative Period in Cases of Pulmonary Resections and Thoracoplasties**

V. O. BJÖRK and H. J. HILTY. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **27**, 455–467, May, 1954. 13 figs., 7 refs.

In this report from the Sabbatsberg Hospital, Stockholm, the authors describe the changes observed in the arterial oxygen and carbon dioxide tension (pO_2 and pCO_2) during the immediate postoperative period in patients undergoing pulmonary resection with and without the addition of thoracoplasty. In most cases measurements of pO_2 and pCO_2 were carried out during voluntary hyperventilation by the patient for about 25 seconds to determine how soon after the operation an effective hyperventilation could be performed.

It was found that after pneumonectomy there was decreased arterial oxygen tension for one week, whether

the resection was performed under an old thoracoplasty or not. In patients subjected to resection of lobes and segments under a thoracoplasty the preoperative arterial oxygen tension was reached within 2 weeks in 9 of 16 cases. In one case in which a five-rib thoracoplasty with apicolysis was performed a considerable decrease in pO_2 was found during the postoperative period (for over 3 weeks). The cause of this was thought to be pain, paradoxical movements of the chest wall, and compression atelectasis.

In general, prolonged impairment of pO_2 was found whenever lobectomy or segmentectomy was performed at the same time as a thoracoplasty. To prevent paradoxical movement of the chest wall the authors have devised a method of thoracoplasty in which the ribs are fixed to the uppermost intact rib by sutures through drill holes. *A. I. Suchett-Kaye*

1334. **The Alveolo-capillary Block Syndrome.** (Het alveolo-capillaire block-syndroom)
H. DEENSTRA and J. G. ROOSENBURG. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **98**, 1150–1156, April 24, 1954. 12 refs.

The authors describe and discuss a possibly new syndrome which they have termed " alveolo-capillary block of unknown origin " and of which 7 cases have been seen at Utrecht University Medical Clinic in the last few years. The condition is characterized by dyspnoea with no apparent cause, a fine mottling in radiographs of the lung, a slow rate of progress, an arterial blood oxygen saturation which is normal or only slightly below normal at rest but falls rapidly on exertion, and in some cases the late development of cor pulmonale with clubbing of the fingers.

Cases in some respects similar to these have been described by workers in the U.S.A. as " acute lung fibrosis ", but the course in those cases was much more rapid and often fatal. The essential mechanism in both groups is thought to be alveolo-capillary block, and the biochemical evidence and lung function tests on which this view is based are described. Various conditions considered capable of producing a similar picture are considered, but the nature of the involvement of the pulmonary vessels which is thought to occur is unknown. *R. Crawford*

1335. **The Pulmonary Alveolar Mucoid Film and the Pneumonocytes**
C. C. MACKLIN. *Lancet* [*Lancet*] **1**, 1099–1104, May 29, 1954. 1 fig., 40 refs.

The pneumonocytes (also called niche cells, septal cells, epicytes, alveolar cells, and a variety of other names) are the characteristic cells of the lung and are presumably of endodermal origin. There are three varieties of pneumonocyte—granular, phagocytic, and membranous, and from a variety of histological evidence reviewed in this paper it is deduced that the granular pneumonocytes produce a mucoid film about 0·2 μ thick which lines the interior of the alveoli. This film is cohesive, flexible, and viscous and probably has many functions, such as the removal of fine particulate matter and organisms, the inhibition of air-bubble formation, and the protection of the underlying tissues from desiccation. There is good evidence that water is contributed to the film by the plasma and evaporates into the alveolar air. The film is probably supported by the membranous pneumonocytes. *J. Naish*

1336. **The Treatment of Non-tuberculous Bronchial Obstruction with Trypsin Aerosols.** (Traitement des obstructions bronchiques non tuberculeuses par des aérosols de trypsine)
A. BIRON and L. CHOAY. *Presse médicale* [*Presse méd.*] **62**, 719–720, May 8, 1954. 29 refs.

The authors report good results obtained from the use of trypsin, the proteolytic enzyme of the pancreas, for the relief of bronchial obstruction due to a plug of mucus, pus, or debris in such conditions as bronchiectasis, asthmatic bronchitis, paroxysmal bronchial asthma, and pulmonary collapse. In their method 250 mg. of trypsin is dissolved in 10 ml. of phosphate solution at *p*H 7, to which is added immediately before use 4 drops of a bronchial muscle relaxant such as 1% isoprenaline sulphate. The solution so prepared is given as an aerosol through a spraying apparatus capable of vaporizing the 10 ml. of liquid in one hour. In the majority of cases a course of treatment in which 5 ml. (125 mg. of trypsin) was given twice a day for 2 days was found to be sufficient.

In all, 80 patients have so far been treated. Excellent results were obtained in 31 out of 33 cases of acute pulmonary collapse, in 12 out of 15 cases of bronchiectasis, in 8 out of 11 cases of asthmatic bronchitis, and in 15 out of 21 cases of bronchial asthma. In some cases treatment with trypsin was given as a preliminary to bronchial aspiration, when the latter was indicated on grounds of emergency. Trypsin has no harmful effects on the bronchial mucous membrane, and only occasionally have minor side-effects resulted, such as temporary hoarseness of the voice, pyrexia, slight dyspnoea, or a temporary fall in the blood pressure. These effects can usually be overcome or prevented by the use of appropriate antihistamine drugs. *A. I. Suchett-Kaye*

INFLAMMATORY DISEASES OF THE LUNG

1337. **Some Relations between Pulmonary Edema and Pulmonary Inflammation (Pneumonia)**
E. D. ROBIN and E. D. THOMAS. *Archives of Internal Medicine* [*Arch. intern. Med.*] **93**, 713–724, May, 1954. 5 figs., 14 refs.

The authors discuss the question whether the well-known association of pulmonary oedema and pneumonia, often seen at necropsy and hitherto dismissed as a " terminal " manifestation, is not perhaps more than coincidental. They have therefore examined the clinical histories and necropsy reports of all fatal cases of pneumonia, pulmonary oedema, or both occurring at the Peter Bent Brigham Hospital, Boston, in the 10-year period 1942–52.

From this clinical and post-mortem evidence they conclude that pulmonary oedema favours the development of pneumonia, and that pneumonia is often accompanied by an inflammatory pulmonary oedema. The difficulties in the clinical and radiological differentiation of these two states, which may occur separately but may also co-exist, are illustrated by a number of case records. Since the pneumonia may be " silent ", prophylactic chemotherapy is advised for all patients with pulmonary oedema. Conversely, patients with pneumonia should be carefully watched and treated at once for the pulmonary oedema should it supervene.

J. Naish

1338. **Acute Bronchopulmonary Suppuration: Therapy with Endoscopic Application of Oleaginous Penicillin**
A. A. CARABELLI. *Diseases of the Chest* [*Dis. Chest*] **25**, 316–327, March, 1954. 12 figs., 13 refs.

In this paper on acute bronchopulmonary suppuration, which was read before the Second International Congress on Diseases of the Chest of the American College of Chest Physicians in August, 1952, the author expresses the view that many conditions at present rather loosely described in such terms, for example, as " unresolved pneumonia ", " chronic suppurative pneumonitis ", or " partial atelectasis " are due to disturbances of the normal function of a lung segment secondary to intrinsic or extrinsic bronchial block from various causes. The pathological changes produced by block are first atelectasis (regarded as reversible), then coagulation of the retained material with solidification of the segment and an associated interference with lymphatic and venous circulation. Fibrosis will finally develop. An acute or chronic lung abscess may be produced, or destruction of muscle, cartilage, and elastic tissue may result in bronchiectasis.

The first phase has been treated at St. Françis Hospital, Trenton, New Jersey, by the introduction into the affected bronchus of oleaginous penicillin, for which purpose a special applicator which can be fitted to a standard Luer–Lok syringe was designed. The applicator is 50 cm. long and 2 mm. in diameter; it is curved to permit unimpeded vision and has a tip of the " velvet eye " type to render it atraumatic. For more inaccessible sites a second applicator was designed with a curved spiral tip. During bronchoscopy the affected bronchus is identified by the pus oozing from its orifice. Some 2 or 3 ml. of penicillin, representing 600,000 to 900,000 units, is introduced into the bronchus, the tip of the applicator being gently advanced until it is stopped; no force is used.

Treatment by instillation of oleaginous penicillin was given to 10 patients suffering from bronchopulmonary suppuration of the segmental type, all of whom had previously received penicillin treatment. In all cases there was immediate improvement. In most of them the temperature fell almost to normal on the following day, and radiological examination usually showed clearing of the lesions in one week. Mild segmental bronchiectasis was diagnosed in one of 6 patients subjected to follow-up bronchography. *T. M. Pollock*

1339. **Bronchographic Studies in Bronchiectasis before and after Pulmonary Resection**
J. A. CRELLIN, J. S. LEHMAN, D. MASON, and J. L. CURRY. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 657–672, May, 1954. 13 figs., 2 refs.

The authors present an analysis of the pre- and postoperative bronchographic findings in 44 cases of bronchiectasis in patients undergoing pulmonary resection at Hahnemann Medical College Hospital, Philadelphia. They have observed that bronchiectasis may occasionally appear after resection in segments of lung which were free from bronchiectasis before operation. The interval elapsing between operation and the postoperative bronchographic examination varied from 5 months to 2 years.

The preoperative findings are discussed, and the frequency of involvement of the various segments is analysed. Study of the postoperative bronchograms showed that the extent and degree of rearrangement of the bronchial tree following resection was directly proportional to the volume of lung removed. In 25 of the 44 cases no evidence of bronchiectasis in the operated lung was demonstrated. Of the remaining 19 cases, 4 showed bronchiectasis due to persistence of a pulmonary segment thought to have been removed, and 4 showed bronchiectasis due to complications (empyema with bronchopleural fistula). In a further 10 cases bronchiectasis appeared in segments previously considered normal in the preoperative period, and these cases are described in some detail.

The possible causes of the appearance of " new " bronchiectasis in the postoperative period are discussed. It is thought that (1) in some cases the bronchiectasis may have been undetectable preoperatively by present techniques; (2) the rearrangement and distortion of bronchi resulting from surgery may impair bronchial drainage; (3) spread of infection from bronchiectasis of the opposite lung in cases of bilateral disease may be a factor. In the authors' experience, in cases in which all but a single segment of a lobe has been removed, the bronchi of the remaining segment may be severely distorted. Such segments have been shown to become more readily the site of bronchiectasis in the postoperative period.

The article is well illustrated with reproductions of bronchograms showing the changes in the distribution of the bronchial tree after resection. *J. Taubman*

1340. **Sulfonamides and Antibiotics in the Treatment of Pneumonia. A Statistical Analysis.** [In English]
P. PELTOLA. *Annales medicinae internae Fenniae* [*Ann. Med. intern. Fenn.*] **43**, 133–151, 1954. 11 figs., 27 refs.

A statistical investigation was undertaken at the Kivelä Hospital, Helsinki, to assess the effects on mortality from pneumonia of the introduction of specific treatment by sulphonamides and antibiotics. General mortality statistics for Finland as a whole were based on death certificates issued since 1927. Mortality statistics for the city of Helsinki were available from 1890, and statistics on the incidence of pneumonia in Helsinki from 1900. A total of 5,241 clinical cases of

pneumonia treated at Kivelä Hospital between 1936 and 1951 were analysed. The group included pure and complicated cases of pneumonia treated with and without sulphonamides, penicillin, aureomycin (chlortetracycline), and chloramphenicol.

In Finland as a whole mortality from pneumonia fell with the introduction of sulphonamides, but since there had been a steady decline in the incidence of pneumonia in Helsinki since 1900 this decrease is not apparent in the mortality statistics for that city. Among the hospital cases studied a greater number of complicated cases had occurred since specific therapy was introduced, and this has kept the total mortality at a high level. Among uncomplicated cases the mortality in all age groups fell markedly with the introduction of sulphonamides, and even farther with that of the antibiotics. There has been an increase in the number of cases in the older age groups in recent years, more marked in Helsinki than in the rest of Finland, and this has had the effect of raising the total mortality figure of the hospital cases in spite of improved therapeutic results. The incidence of bacterial complications due to septicaemia notably declined, but that of other complications less so. Where pneumonia was complicated by other diseases, such as diabetes, specific therapy has clearly shown its effectiveness. In spite of this, however, the length of stay of patients in hospital has been little altered.

[This paper demonstrates that comparative studies are valid only within one and the same group.]

Ronald S. McNeill

1341. **The Surgical Treatment of Hydatid Cysts of the Lung: a Series of 100 Cases.** (Les kystes hydatiques du poumon. Leur traitement chirurgical d'après 100 observations)

P. GUEDJ. *Journal de chirurgie* [*J. Chir.* (*Paris*)] **70**, 393–411, May, 1954. 15 figs., 35 refs.

As a result of his experience of hydatid disease in an agricultural community in Algeria the author has devised, and here describes, a technique which is applicable to the removal of most pulmonary hydatid cysts, whether they are simple or complicated, single or multiple. Other techniques are discussed and the objections to them detailed. He condemns the old two-stage method of cyst drainage because of its often high incidence of pleural complications. He also objects to the delivery of the intact cyst through an incision in the lung on the grounds that the incision may have to be very large and also that there is a risk of rupture of the cyst, with resultant pleural contamination from the latent sepsis which almost always exists in the cyst wall. He has found this infection to be present in most cases which he has examined bacteriologically. There is the further objection that plication and obliteration of the residual cavity must be carried out blindly, distorting the remaining lung tissue and possibly damaging vessels, resulting in haemorrhage, and is to be condemned.

The author therefore suggests that most cysts can be treated in the following manner. With adequate exposure through a large thoracotomy, the cyst is located and the fluid aspirated very slowly after the method of Barrett. An incision of not more than 4 or 5 cm. is then made in the shell of lung overlying the cyst, and through this the fragile cyst-wall is gently removed with the aid of the aspirator. The incision in the lung is closed around a fine catheter, which is then led out to an underwater seal. The pleura is also drained through a separate tube through which suction at a pressure of 20 cm. of water is immediately applied. The small pulmonary tube usually drains 40 to 50 ml. of blood-stained serum and can be removed in about 6 days or when there is no longer radiological evidence of fluid in the space; the pleural drain may be removed in 4 or 5 days. No attempt is made to suture bronchi or excise the adventitial membrane.

This method has been employed in 51 cases, with good results in 46; in one case there were pleural complications, in 2 residual cavities, and 2 patients died. Among the patients successfully treated was one in whom 9 cysts were removed at one session from one lung, and another in whom there was evidence of earlier spontaneous rupture of the cyst, only the cyst wall being retained.

In the author's opinion resection should be reserved for small cysts situated in relation to the costo-phrenic sulcus, where drainage is difficult, for suppurating cysts associated with gross bronchiectasis, for cases of secondary haemorrhage from a residual cavity, and lastly when there is secondary invasion by the tubercle bacillus. Case histories illustrative of these conditions are appended.

A. M. Macarthur

1342. **Medical Management of Acute Lung Abscess**

S. A. GITTENS and J. P. MIHALY. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 673–681, May, 1954. 5 figs., 3 refs.

Before the advent of chemotherapy many cases of acute abscess of the lung relapsed into chronicity or, because of subsequent complications, became surgical problems. In this paper the authors describe the management of 37 patients treated for acute, uncomplicated lung abscess at Harlem Hospital, New York, between April, 1949, and April, 1952. All were admitted within 10 days of the onset of illness, and treatment consisted in administration of either penicillin alone or penicillin plus sulphadiazine, chlortetracycline (aureomycin), or oxytetracycline (" terramycin "); other combinations of these drugs were used if response was slow. The criteria of cure are defined. The " clinical cure time " was the time taken to reverse signs and symptoms of toxicity, to diminish sputum output to less than 30 ml. daily, and to produce the first radiological evidence of clearing; this period averaged 24 days. The " total cure time " was the clinical cure time plus the time required to achieve complete radiological clearing, with the exception of fibrotic residues; this time averaged 60 days.

Of the 37 patients, 10 received sulphadiazine (1 g. 4 times daily) plus penicillin (600,000 units) and their average total cure time was 67·7 days. In 3 cases given penicillin only the average time was 35 days; in 12 given chlortetracycline, 64·3 days; and in 6 given oxytetracycline, 69 days. In some cases the drugs were changed during the course of treatment.

There were no complications in the series. Although the number who received penicillin only was very small, the authors conclude that penicillin is just as effective in the treatment of abscess of the lung as the tetracycline series of drugs, at least where the abscess is due to the usual pathogenic organisms [but the bacteriological findings are not given in detail]. The tetracycline drugs produce a less rapid response, but they may succeed where penicillin has failed and the authors therefore recommend the tetracycline drugs in such cases or when cultures show that the organism is resistant to penicillin. Chlortetracycline and oxytetracycline appeared to be equally efficacious in this series. *J. Taubman*

NEOPLASTIC DISEASES

1343. **Assessing the Inoperability of Bronchial Carcinoma by Angiocardiography**
B. V. SLESSER, R. G. BRITT, and J. L. FREER. *Thorax* [*Thorax*] **9**, 91–99, June, 1954. 11 figs., 5 refs.

With a view to establishing the value of angiocardiography in assessing the operability of cases of bronchial carcinoma this procedure was carried out at the Leicester Chest Unit in 31 cases of the disease, all of which were adjudged operable on clinical and bronchoscopic grounds. The patient was prepared with "omnopon" and scopolamine, and 50 ml. of 70% diodone solution injected as rapidly as possible through a wide-bore cannula into the antecubital vein, with the patient supine. Eight films were then exposed in 10 seconds with the aid of an automatic serial changer.

Criteria of inoperability were: (1) partial obstruction or irregular filling of, or filling defects in, the superior vena cava or left innominate vein and associated back pressure in the small venous tributaries not normally demonstrable; (2) partial or complete occlusion or irregular filling of the main right pulmonary artery proximal to its bifurcation; and (3) partial or complete occlusion or deformity of the main left pulmonary artery within 1·5 cm. of its origin from the common pulmonary trunk. Displacement, deformity, and partial or complete occlusion of the branches of the main arteries are not considered to indicate inoperability, although they may suggest that intrapericardial ligation of the main vessel might be needed; nor need displacement of the superior vena cava by enlarged mediastinal nodes be regarded as necessarily a sign of inoperability.

In the 31 cases investigated there were 11 instances where angiocardiography suggested, on the basis of the above criteria, that the growth would be inoperable, and thoracotomy confirmed these findings. (In 3 cases there was deformity of the superior vena cava, and in 8 deformity of the main pulmonary artery.) In the remaining 20 cases the angiocardiograms showed normal great vessels or block or deformity of the branch vessel only, and these cases were found to be operable at thoracotomy.

The authors are of the opinion that angiocardiography will prove especially valuable in cases of hilar carcinoma, where resection may be impossible owing to mediastinal invasion, and that if used in conjunction with other routine procedures in assessing operability fewer unnecessary (and perhaps harmful) thoracotomies will be undertaken. *F. J. Sambrook Gowar*

1344. **Bronchogenic Carcinoma in Young Men**
A. E. ANDERSON, H. A. BUECHNER, I. YAGER, and M. M. ZISKIND. *American Journal of Medicine* [*Amer. J. Med.*] **16**, 404–415, March, 1954. 5 figs., 23 refs.

It has long been recognized that age influences the incidence and behaviour of neoplastic disease. The present authors have analysed the findings in 30 cases of bronchogenic carcinoma seen at the Veterans Administration and Charity Hospitals, New Orleans, since 1944, all the patients being males under 40 years of age. In 28 cases the diagnosis was confirmed histologically. In the majority the primary lesion was located peripherally in the lung, chest pain being a frequent presenting symptom. Pulmonary symptoms were comparatively rare, the carcinoma being discovered at routine examination for the cause of other symptoms, which were frequently neurological and due to cerebral metastases. Bronchoscopy was negative [not surprisingly] in 19 out of 23 cases, the diagnosis being established only at exploratory thoracotomy or at necropsy. Histological examination revealed adenocarcinoma in 11 cases, undifferentiated carcinoma in 11, and squamous-celled carcinoma in 5; in 3 cases the type of tumour was not determined. In most of the cases the tumour grew and metastasized rapidly. The average duration of life from the onset of symptoms was 14 months [but this is affected by a few extremes in what amounts to a small series of cases; excluding these, the mean survival was 7·5 months]. The findings in these cases are in marked contrast with those in cases of bronchogenic carcinoma in older subjects, and the authors discuss several theories of aetiology, such as the presence of congenitally maldeveloped bronchial buds with inherent instability, as opposed to exposure to irritants, which cause squamous-celled tumours. *Ronald S. McNeill*

1345. **Bronchial Carcinoma—A Pandemic**
J. CLEMMESEN. *Danish Medical Bulletin* [*Dan. med. Bull.*] **1**, 37–46, April, 1954. 14 figs., 35 refs.

The registration of cases of cancer is more highly developed in Denmark than in any other country and the author, writing from the Danish Cancer Registry, Copenhagen, has taken advantage of the elaborate data which are now available to study a number of problems of world-wide interest concerning the epidemiology of cancer of the lung.

His first important conclusion is that while there is no reason to suppose that the real mortality from this cause has increased in women (at least not in Denmark, Holland, or Norway), the disproportionate increase in mortality which has taken place among men does reflect a real increase in the incidence of the disease. He suggests that atmospheric pollution cannot be of aetiological importance since: (1) the greater mortality from lung cancer in the capital as compared with Danish provincial towns and rural areas is largely confined to men; (2) the mortality among men in Copenhagen is greater

in those parts of the city characterized by low house-rents, irrespective of the location of these districts within the city; and (3) the age distribution of the disease has changed as the mortality has increased, and moreover has changed in such a way as would be expected if men born at different periods had experienced different degrees of exposure to an environmental carcinogen, and not as would be expected if the changes in the environment had affected persons of all ages equally.

A study of the changes in mortality which have affected different age cohorts leads to the conclusion that the age distribution of patients with lung cancer will eventually have the same characteristics as are found in other types of extra-genital cancer, and that by 1990, when this will have occurred, the annual number of deaths from cancer of the lung among males will be more than the present recorded number of deaths from all forms of cancer. The increase in mortality among men did not begin in Copenhagen until about 1935. The author is of the opinion that the subsequent trends accord with the introduction of a new carcinogenic influence in the first two decades of the present century, affecting young men, and with an average latent period of about 20 years. The present differences in incidence between men and women and between town and country would be accounted for if the carcinogenic influence began to affect the different groups at different periods.

In the author's opinion the Danish epidemiological evidence is consistent with the view that the main aetiological factor in bronchial carcinoma is cigarette smoking—the direct evidence for which he has reviewed elsewhere (Clemmesen and Jensen, *Ugeskr. Læg.*, 1953, **115**, 1565). He concludes with the warning that in the spread of lung cancer we are now facing one of the major catastrophes of medical history, and strongly urges that, as interim measures, (1) " the younger generation must be prevented from adopting the exaggerated smoking habits of the present generation ", and (2) the addition of filter-tips to cigarettes should be made compulsory.

R. Doll

1346. **Carcinoma of the Bronchus Presenting as Thin-walled Cysts**

H. J. ANDERSON and J. W. PIERCE. *Thorax* [*Thorax*] 9, 100–105, June, 1954. 11 figs.

In this paper from St. Thomas's Hospital, London, are described 6 cases of squamous-cell bronchial carcinoma in which the radiological appearances were those of a thin-walled cavity or cyst. The cavities were 1 to 3 inches (2·5 to 7·5 cm.) in diameter, the smaller ones being round and the larger ones oval or irregular. There was no surrounding consolidation or fluid level, and the appearances were unlike those of a breaking-down squamous-cell carcinoma. On section the lining of the cavity was smooth, grey, and shining in parts, but rough and opaque where superficial inflammation was present. In 2 cases a small nodule of growth and fibrous tissue was present at the junction of the cavity with its communicating bronchus. On microscopical examination the cavity was seen to be lined in part by a flattened layer of malignant cells and in part by compressed lung tissue or flattened metaplastic squamous epithelium with the malignant tissue spreading just beneath the surface. There was no evidence of extension of growth into the surrounding lung, nor of degeneration of the malignant cells in the cavity wall.

The authors consider that this variety of bronchial carcinoma arises by the ingrowth of a thin layer of malignant cells to line a pre-existing cavity, the cavity being due to valvular bronchial obstruction by a small nodule of growth or by inflammatory changes in the vicinity of the neoplasm. *F. J. Sambrook Gowar*

1347. **The Fate of Patients with Alveolar-cell Tumor of the Lungs**

T. W. MEARS, J. W. KIRKLIN, and L. B. WOOLNER. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **27**, 420–424, April, 1954. 1 fig., 7 refs.

After describing the macroscopic and microscopic features of alveolar-cell tumour of the lung and discussing the theories of its origin, the authors review 13 cases of this condition treated by them at the Mayo Clinic, 10 in women and 3 in men, the patients ranging in age from 30 to 66 years, with an average age of 51·8 years.

Three patients had no chest symptoms when they were first examined, the average duration of symptoms in the remaining 10 patients being 11½ months. The commonest symptoms were cough, dyspnoea, fever, pain in the chest, and haemoptysis. In all cases the lesion was demonstrated radiologically, but in none could the finding be regarded as diagnostic. The authors state that *x*-ray examination may show a small, poorly defined area of consolidation simulating pneumonitis. As the disease progresses other portions of one or both lungs may become involved. In the advanced stages both lungs are involved, with multiple foci which frequently become confluent and give the appearance of a mass or of a consolidated lobe.

The usual significant finding at bronchoscopy was a frothy mucoid sputum coming from the involved segments of the lung. Either the bronchial washings or the sputum (or both) were positive for malignant cells in 7 of the 11 cases in which cytological examination was carried out. It is advised that the sputum be examined postoperatively for malignant cells to ascertain whether all the involved lung tissue has been removed.

Although the results of treatment have been very disappointing, the authors consider that the only method of even palliative value at the present time is conservative resection of the affected portion of the lung. Lobectomy was performed in 10 cases and pneumonectomy in 3. Two patients needed a second operation—in one, completion of pneumonectomy after left upper lobectomy; in the other, right upper lobectomy following left lower lobectomy. There were 2 operative deaths. Only 4 of the 13 patients are still alive, and 2 of these have evidence of recurrence; the other 2 have survived one year and 4 years respectively without evident recurrence.

F. J. Sambrook Gowar

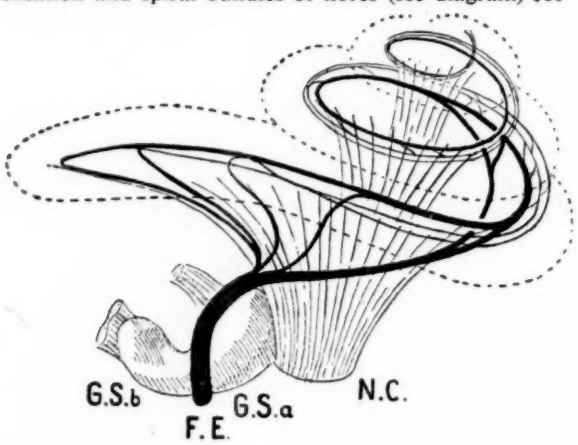
1348. **Sarcoma of the Lung**

T. H. NOEHREN and F. W. MCKEE. *Diseases of the Chest* [*Dis. Chest*] **25**, 663–678, June, 1954. 5 figs., 41 refs.

Otorhinolaryngology

1349. **Efferent Nerve Fibers of Cochlea**
M. PORTMANN and C. PORTMANN. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **59**, 543–554, May, 1954. 8 figs., 24 refs.

It is now known that, as well as the sensory terminals of the cochlear nerve, there exist in the ganglion of Corti spiral bundles of fibres the nature of which is not yet understood. Bocca believes that they are essentially sensory fibres and that their function is concerned with the spatial quality of sound, as Kobrak also has suggested. This means that there is a double sensory innervation of the cochlea—radial fibres for ordinary acoustic sensation and spiral bundles of fibres (see diagram) for



General diagram of cochlear spiral efferent bundles (in heavy black). N.C., cochlear nerve; F.E., efferent bundle studied; G.S.*a*, Scarpa's ganglion, saccular portion; G.S.*b* Scarpa's ganglion, utriculo-ampullar portion.

the spatial quality of sound. Fernandez and the present authors consider that the spiral bundles are made up almost entirely (98%) of efferent fibres, which originate in the medulla and pass with the nerve and through the vestibular ganglion. Thus the radial system is sensory or afferent, the spiral efferent.

The authors describe in the inner ear the following groups of fibres: (1) the cochlear fibres; (2) vestibular fibres; (3) fibres of the postganglionic portion of the ortho-sympathetic system terminating in the walls of the vessels; and (4) other fibres, grouped in bundles, staining differently from the other groups, and showing large numbers of Schwann nuclei. These fibres arise in a nucleus in the region of the superior olive and have been traced to the vestibular ganglion, which they pass without any relay. The authors believe that the bundle corresponds to the vestibulo-cochlear anastomosis of Oort. The fibres cross the ganglion of Corti, again without relay, and form the spiral bundles of this ganglion. They terminate under the inner hair cells of Corti's organ. In favour of the view that they are efferent fibres are the following facts: they have no cell bodies in their course as they pass through the ganglia of Scarpa and of Corti; they have the histological characters of efferent fibres; they remain unchanged when the rest of Corti's organ degenerates under prolonged acoustic trauma.

The function of these fibres is still undecided, but their structure and arrangement make it improbable that they are parasympathetic nerves. *F. W. Watkyn-Thomas*

1350. **Surgery of the Sympathetic in Ménière's Disease, Tinnitus Aurium, and Nerve Deafness. A New Concept in Acute Fulminating Ménière's Disease**
L. F. JOHNSON. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **59**, 492–498, April, 1954. 15 refs.

The surgical methods here described are based largely on Passe's work on the surgery of the sympathetic nervous system for inner ear conditions (*Proc. roy. Soc. Med.*, 1951, **44**, 760; *Abstracts of World Surgery*, 1952, **11**, 37). The most interesting point in the paper is the author's suggestion that cases of sudden, acute deafness of cochlear type, which he describes as " acute fulminating Ménière's disease ", should be treated within a few hours of onset as a surgical emergency. There is a possibility, he argues, that in these cases (which sometimes occur without vertigo) there is an endolymphatic hydrops which may produce irreversible change unless quickly relieved. In such cases procaine block of the stellate ganglion is a possible method of relief. If temporary relief is given by stellate block, it is then justifiable to perform dorsal sympathectomy. This has been successful in a number of cases, but is of no avail in traumatic tinnitus due, for example, to explosion. *F. W. Watkyn-Thomas*

1351. **Chronology of the Sphenoidal Sinus and its Value in Diagnosis**
G. MARAÑÓN and F. GALVEZ ARMENGAUD. *British Medical Journal* [*Brit. med. J.*] **1**, 778–779, April 3, 1954. 1 fig., 4 refs.

The chronological development of the sphenoidal sinus and its significance in diagnosis are discussed. At the General Hospital, Madrid, a study of a large number of radiographs of the skull, including 365 from healthy subjects aged 3 to 19 years and a much larger number from children suffering from various pathological conditions, showed that the sphenoidal sinus is the least variable of the accessory sinuses, and that a definite chronology of development can be observed. The sinus is first seen at the age of 3 to 3½ years as a small vesicle situated far in front of the sella turcica. At 8 years it is well defined and has reached the anterior plane of the sella, while at 16 it has reached the posterior plane of the sella turcica; normally the sphenoidal sinus ceases to grow after the age of 16. In pituitary insufficiency development is arrested at some point before this final stage is reached. The degree of underdevelopment is roughly proportional to the degree of pituitary insufficiency. *S. A. Beards*

Endocrinology

THYROID GLAND

1352. **Potency and Duration of Action of Triiodothyronine and Thyroxine in Rats and Mice**
B. G. ANDERSON. *Endocrinology* [*Endocrinology*] **54**, 659–665, June, 1954. 5 figs., 8 refs.

The potency and duration of action of L-triiodothyronine and of DL-thyroxine were compared by determining their effects on the release of ^{131}I from the thyroid in rats and on the sensitivity to anoxia in mice. Triiodothyronine appeared to be from five to ten times as active as DL-thyroxine by each method. No significant difference in latent period or duration of action was shown in mice following single injections and tested over a period of 72 hours. DL-Thyroxine appeared to exert a more prolonged effect than triiodothyronine in suppressing the release of ^{131}I from the thyroid in rats when doses of similar potency were compared.—[Author's summary.]

1353. **Evaluation of the Antithyroid Activity of 5-Iodo-2-thiouracil**
R. C. GOLDBERG and J. WOLFF. *Endocrinology* [*Endocrinology*] **54**, 181–195, Feb., 1954. 8 figs., 30 refs.

Experiments were performed at the Harvard School of Dental Medicine and Harvard Medical School, Boston, Massachusetts, to assess the antithyroid activity and non-goitrogenic properties of 5-iodo-2-thiouracil (ITU) in the rat. The results obtained were as follows.

1. There was a very slight reduction in the oxygen consumption of surviving liver and kidney slices from rats which had received 0·16 or 0·2% ITU in the diet for 7 weeks. There was no thyroid hyperplasia, and cytological examination of the hypophysis showed no degranulation of alpha cells, thus indicating that thyroid hormone synthesis was not completely blocked.

2. The uptake of radioactive phosphorus by the thyroid (considered to be a reliable index of thyrotrophic stimulation) was less in the ITU-treated rats than in those given propylthiouracil (PTU).

3. As the above experiments showed that 0·16 or 0·2% ITU had much less antithyroid activity than PTU, higher doses were tried. With 1% ITU given for a month the thyroid became grossly hypertrophied and cytologically indistinguishable from that of PTU-treated rats. In the pituitary there was complete degranulation of alpha cells. It was therefore concluded that higher doses of ITU produce a complete inhibition of thyroid activity, but have a marked goitrogenic action.

4. Assessment of thyroid activity by measuring the rate of release of organic ^{131}I by the gland showed that ITU had the same accelerating effect as 0·1% thiouracil (TU) only when given in goitrogenic doses (1%). The rate of release of organic ^{131}I by rats treated with 0·2% ITU was very slightly above that of a control group of untreated rats.

5. ITU had less effect in decreasing the thyroid iodine content than did TU alone, 1% ITU producing a decrease in the organic iodine content similar to that obtained with 0·1% TU. On the other hand, it actually increased the total thyroid iodine content.

6. The simultaneous administration of 0·025% TU and equimolar iodide produced effects similar to those obtained by giving non-goitrogenic doses of ITU. This is regarded as suggesting that the anomalous action (antithyroid but not goitrogenic) of ITU might be due to the combined action of its breakdown products, thiouracil and iodine. *Richard de Alarcón*

1354. **Clinical Correlation of Pretibial Myxedema with Malignant Exophthalmos**
W. H. BEIERWALTES. *Annales of Internal Medicine* [*Ann. intern. Med.*] **40**, 968–984, May, 1954. 6 figs., 7 refs.

The incidence of localized pretibial myxoedema in association with malignant exophthalmos was studied in a group of 28 patients being followed up after treatment for the latter condition at the University Hospital (University of Michigan), Ann Arbor. It was found that 7 of the 28 patients had pretibial myxoedema. No difference was observed between the two groups—that is, those with and those without pretibial myxoedema—as regards age and sex of the patients, duration of exophthalmos, presence or absence of thyrotoxicosis, and the treatment given for the thyrotoxicosis. The pretibial area involved increased with the duration of the myxoedema; moreover, there was no regression of the lesions in this area with treatment of the exophthalmos.
F. W. Chattaway

1355. **The Thyro-hypophysial Syndrome. I. The Primary Reaction of the Hypophysial Eye Signs (Including Exophthalmos) to the Treatment of Thyrotoxicosis.** [In English]
B. A. LAMBERG. *Acta medica Scandinavica* [*Acta med. scand.*] **148**, 225–237, 1954. 3 figs., bibliography.

An investigation was carried out at the Maria Hospital (University of Helsinki), to determine whether the clinical signs of exophthalmos which are present initially in cases of hyperthyroidism can be correlated with the eye changes occurring in association with subsequent treatment. The degree of exophthalmos was measured with careful precautions by means of a Hertel exophthalmometer before treatment and at intervals afterwards. The mean of 6 to 10 separate readings was taken, and a change of 0·25 mm. in this mean was considered significant.

It was found that one of the first results of medical treatment of thyrotoxicosis, regardless of whether a drug of the thiouracil group or potassium iodide was given, was a rapid increase in the degree of exophthalmos; the onset often coincided with clinical improvement and a

decrease in the basal metabolic rate. In some cases thyroidectomy at this stage was followed by a further increase, either rapid or prolonged; in others no such exacerbation was observed. Postoperatively the degree of exophthalmos tended to increase in those cases in which swelling of the eyelids or filling of the upper orbitopalpebral sulcus was present before treatment. In individual cases these clinical signs appeared to be of greater importance than the initial exophthalmometer reading.

G. A. Smart

1356. **A Four-year Study of the Treatment of Hyperthyroidism with Methimazole**

T. H. McGavack, J. Chevalley, S. Kenigsberg, and S. Pearson. *Bulletin New York Medical College, Flower and Fifth Avenue Hospitals* [*Bull. N.Y. med. Coll.*] **16**, 58–85, 1953. 37 refs.

The results of the administration of methimazole for periods of 14 days to 4 years to 184 patients aged 15 to 83 years with hyperthyroidism are described in this paper from New York Medical College. The initial daily dose of methimazole was 15 to 60 mg. and the maintenance dose 2·5 to 30 mg., the majority of the patients requiring about 20 mg. daily for a steady continuous effect. Iodine in the form of Lugol's solution in a daily dose of one minim (0·06 ml.) was given when the patient became euthyroid.

Provided the dosage of methimazole was adequate, subjective and objective improvement was obtained in three-quarters of the patients within one week of the start of treatment, 85% becoming euthyroid within 5 weeks. Of the 184 patients 29 relapsed with symptoms of hyperthyroidism within 4 months of cessation of therapy, while 8 showed symptoms after a period of freedom of at least 4 months. In 37 cases methimazole was given only in preparation for thyroidectomy. Of the remaining 147 patients, a satisfactory follow-up was obtained in 96, 41 of whom were still being actively treated. Treatment was complete in 55, and of these 34 remained symptom-free for an average of 15 months after administration of the drug was stopped.

Toxic reactions, noted in only 8 cases, included pruritus, rashes, urticaria, fever, and granulocytopenia, being severe in one case of drug fever and 2 of granulocytopenia; in the others the toxic effects were moderate or mild and did not preclude the use of other antithyroid drugs. The most severe reactions occurred in patients receiving a daily dose of 40 mg. or more of methimazole.

The authors conclude that methimazole is a rapidly acting, relatively safe, and effective antithyroid drug.

D. G. Adamson

1357. **Goiter due to Lymphocytic Thyroiditis (Hashimoto's Struma). Its Occurrence in Preadolescent and Adolescent Girls**

D. Gribetz, N. B. Talbot, and J. D. Crawford. *New England Journal of Medicine* [*New Engl. J. Med.*] **250**, 555–557, April 1, 1954. 1 fig., 16 refs.

It has long been thought that in pre-adolescent children most non-toxic goitres not due to carcinoma were of the simple colloid type. In the present paper 6 cases of goitre due to chronic lymphocytic thyroiditis of the Hashimoto type occurring in girls aged 9 to 13 are described from the Massachusetts General Hospital, Boston. Only 11 other cases of Hashimoto's struma in children could be found in the literature.

In the present series there was a family history of thyroid disease in 2 cases. The patients had no symptoms, except for a mild dysphagia in one case, but in another child there was considerable retardation of skeletal maturation suggestive of hypothyroidism. The thyroid gland was enlarged to two to four times the normal size, and was firm, easily outlined, and of coarsely granular consistence. In 3 cases the goitre was nodular, in 3 the pyramidal lobes were palpable, and in 3 the Delphian lymph nodes were enlarged. In 4 cases subtotal thyroidectomy was performed; in the other 2 a biopsy specimen was obtained. Microscopical examination showed extensive lymphocytic infiltration, with germinal-centre formation and hyperplasia of the epithelial cells. The serum protein-bound iodine values in 3 out of 5 of the cases were abnormally high—a remarkable finding in view of the absence of symptoms of thyrotoxicosis. Normally the total serum protein-bound iodine comes mostly from thyroxine-like, butanol-extractable, iodinated compounds, which are metabolically active. It seems possible that in thyroiditis the follicles release either partially proteolysed or unproteolysed thyroglobulin or non-calorigenic compounds similar to diiodotyrosine, or both, into the circulation. This is known to occur in certain cases of thyroid carcinoma and in acute radiation thyroiditis.

The patients were treated with generous doses of thyroid extract, which caused shrinking of the goitre. The thyroid extract presumably acted by raising the level of metabolically active thyroid substances, that is, the butanol-extractable iodine, in the circulation. This would tend to suppress the formation of pituitary thyrotrophic hormone, which had previously overacted and produced the goitre, resulting in a reduction in both size and activity of the thyroid gland. *Marianna Clark*

ADRENAL GLANDS

1358. **Interactions between Systemic and Local Stress**

H. Selye. *British Medical Journal* [*Brit. med. J.*] **1**, 1167–1170, May 22, 1954. 1 fig., 23 refs.

Using the granuloma-pouch technique, it was shown that, depending upon circumstances, systemic stress can either inhibit or aggravate the topical damage caused by exposure of a limited tissue area to a pathogen—for example, a chemical irritant, such as croton oil.

The antiphlogistic effect of stress is not merely due to increased secretion of cortisol-like hormones, since it is also observed in adrenalectomized animals maintained on (in themselves inactive) threshold doses of injected cortisol. The aggravation of topical tissue injury by systemic stress also depends only in part upon endogenously produced adrenal hormones; it is abolished by complete adrenalectomy, but not if suitable substitution therapy with antiphlogistic corticoids (cortisone, cortisol)

is given. Both these effects of systemic stress upon topical tissue reactions can be delayed, becoming manifest only after the systemic stressor has ceased to act.

The interrelation between systemic and local manifestations of disease in general are discussed in the light of these findings.—[Author's summary.]

1359. **The Effect of Aldosterone (Electrocortin), a New Adrenal Hormone, in Addison's Disease.** (L'effet d'une nouvelle hormone surrénale, l'aldostérone (électrocortine) dans la maladie d'Addison)
R. S. MACH and J. FABRE. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **70**, 353–359, March 26, 1954. 3 figs., 7 refs.

The authors report, from the University Medical Clinic, Geneva, a study of the action of the new corticoid, aldosterone, in 2 cases of Addison's disease. Both patients also received deoxycortone acetate under similar conditions, and the clinical and metabolic effects were compared.

One hour after the injection of aldosterone the symptoms of adrenal insufficiency had disappeared completely, this beneficial effect lasting for 6 or 7 hours. After a few days of treatment the pigmentation of the skin cleared in a striking and unexpected way. In one case treatment with aldosterone for 6 days had more effect on the pigmentation than several months' treatment with cortisone. The changes in the electrolyte balance were similar to those obtained with deoxycortone acetate, that is, there was retention of sodium and chloride and increased potassium excretion, without, however, affecting the water balance or producing a pathological retention of water. The corticoid had no effect on the blood pressure, although haemodilution tests showed an increase in blood volume. The typical flattened glucose tolerance curve seen in adrenal insufficiency, with a marked secondary hypoglycaemia, reverted to normal after administration of aldosterone, but this effect on carbohydrate metabolism was not obtained with deoxycortone acetate.

Aldosterone is an extremely active hormone, and the authors found the effective dose in Addison's disease to be about 2·5 to 3·3 μg. per kg. body weight. It is thus some 20 to 30 times more active than deoxycortone acetate. Its action in Addison's disease is similar to that of cortisone in so far as it acts on the pigmentation and carbohydrate metabolism, but it has no effect on the leucocytes, particularly eosinophils, or on nitrogen and water metabolism. *Richard de Alarcón*

1360. **Experiences with A.C.T.H. and Cortisone. A Note on Long-term Therapy**
E. H. MCGEHEE and K. MACLEAN. *British Medical Journal* [*Brit. med. J.*] **1**, 1171–1175, May 22, 1954. 15 refs.

The authors' experience at Guy's Hospital, London, during a 2½-year period in the treatment of various diseases with cortisone and ACTH is briefly reviewed. Patients receiving these drugs for the first time were treated for about 3 weeks according to one of the following dosage schedules: (1) 20 to 40 mg. of ACTH daily by slow intravenous infusion for a minimum of 8 and occasionally up to 16 hours; (2) 20 to 40 mg. of ACTH gel daily in a single intramuscular injection; (3) 100 to 200 mg. of cortisone by mouth daily in 4 separate doses; (4) 100 to 150 mg. of cortisone daily in a single intramuscular injection. When it was apparent that the disease was controlled, usually in 7 to 14 days, the daily dose of cortisone was reduced or ACTH was administered on alternate days. Serum sodium and potassium levels were estimated initially, such estimation being repeated only if intensive treatment was continued for more than 2 weeks or the patient's condition required it. When the drugs were given daily, fluid intake was restricted in apyrexial patients to 50 to 60 oz. (1·4 to 1·7 litres) a day. No additional sodium chloride was permitted, but up to 4 g. of potassium chloride was given daily.

The disease conditions in 185 patients are tabulated. Complications included gastrointestinal perforation in 3 cases (the classic early symptoms being masked by the drugs), with 2 deaths; acute psychosis in 3 cases; and steroid diabetes in one case.

The results of long-term out-patient treatment in 44 cases are discussed. Of these 44 patients, 18 had Addison's disease or pituitary dysfunction, 3 polyarteritis nodosa, 2 disseminated lupus erythematosus, one subacute collagen disease, 5 scleroderma, one rheumatoid arthritis, 6 pemphigus, 2 exfoliative psoriasis (response poor), and 6 eye diseases. The results were highly satisfactory; in many of the cases the disease underwent remission so that treatment could be stopped, at any rate for a time. *Norval Taylor*

1361. **Studies of 17-Hydroxycorticosteroids. IV. Evaluation of a Standard ACTH–17-Hydroxycorticosteroid Response Test in Children**
R. S. ELY, R. B. RAILE, P. F. BRAY, and V. C. KELLEY. *Pediatrics* [*Pediatrics*] **13**, 403–411, May, 1954. 1 fig., 30 refs.

Adrenal cortical activity is usually assessed from such factors as the eosinopenic response, urinary excretion of steroids, and water and electrolyte balance. It can be determined more directly by the change in blood level of 17-hydroxycorticosteroids in response to intramuscular injection of ACTH. At the University of Utah College of Medicine, Salt Lake City, adrenocortical function was determined in this way in 40 children suffering from various disorders and in 40 healthy children aged 2½ to 16 years.

Before, and 2 hours after, intramuscular injection of 25 i.u. of ACTH 30 ml. of blood was withdrawn and the plasma level of 17-hydroxycorticosteroids determined by the method of Nelson and Samuels (*J. clin. Endocr.*, 1952, **12**, 519). The eosinophil count was also determined for each subject. In the control group the mean plasma concentration of 17-hydroxycorticosteroids was 12·0 μg. per 100 ml. before administration of ACTH and 29·8 μg. per 100 ml. afterwards. The difference was significant, but there was considerable variation between individuals, both in the initial level and in the degree of response (this variation was lessened somewhat if the

response was assessed on the basis of body weight). Since a very low initial level was observed in several healthy children, the authors consider that this value alone is not an indication of inadequate adrenocortical function. In children with congenital hyperplasia, however, the initial plasma steroid level was consistently low (mean 2·6 μg. per 100 ml.), and there was no significant rise after administration of ACTH.

In 50 cases the observed rise in plasma 17-hydroxycorticosteroid level was compared with the degree of eosinopenia, but no correlation was found, suggesting that the eosinopenia induced by ACTH is not dependent upon an increase in circulating steroids.

In the authors' view this method of determining adrenocortical function has considerable value, but the results of a single test should not be interpreted too rigidly, since both a low initial plasma level of steroids and a poor response to ACTH are observed occasionally in healthy subjects. It is suggested that dosage based on body weight and giving the ACTH intravenously might improve the test by minimizing certain individual variations. *Nancy Gough*

1362. **Levels of 17-Hydroxycorticosteroids in Body Fluids**
A. A. SANDBERG, K. EIK-NES, D. H. NELSON, and F. H. TYLER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **43**, 874–879, June, 1954. 9 refs.

DIABETES MELLITUS

1363. **A Comparison of Insulin Treatment with and without Added Carbohydrate in Human Diabetic Ketosis**
M. ROSECAN and W. H. DAUGHADAY. *Journal of Clinical Investigation* [*J. clin. Invest.*] **33**, 49–56, Jan., 1954. 4 figs., 31 refs.

In order to determine whether the administration of carbohydrate in addition to insulin actually speeds recovery from diabetic ketosis, the authors estimated the fall in the blood ketone level in diabetic ketosis during insulin therapy with and without the addition of carbohydrate. The efficacy of fructose given intravenously in lowering the blood ketone level was compared with that of glucose, since some workers have found that the utilization of fructose in diabetic acidosis is normal.

Ketosis was induced in 8 diabetic patients aged 19 to 67 years by withdrawing insulin for 3 days. In spite of marked polyuria all the patients remained hydrated when given saline and soluble insulin in a dosage sufficient to control hyperglycaemia, but no additional carbohydrate. A solution of 10% glucose or fructose was administered intravenously at the rate of 0·8 g. per kg. body weight per hour for 4 hours, and the blood level and urinary excretion of ketones were measured by the method of Weichselbaum and Somogyi (*J. biol. Chem.*, 1941, **140**, 5).

The rate of fall in the blood level of ketones was significantly greater after administration of fructose and insulin than after saline and insulin in 5 out of 6 patients. The fall in response to fructose and insulin was slightly more rapid than that in response to glucose and insulin, but the difference was not significant. Urinary excretion of ketones tended to decrease as the blood level fell, but there was a poor correlation between the blood level and the urinary excretion of ketones. No significant difference was observed between the average total ketonuria following any of the therapeutic procedures.

The authors discuss 3 factors which might explain the more rapid fall in the blood ketone level when carbohydrate is given: (1) increased renal loss of ketones; (2) increased peripheral utilization of ketones; and (3) a decrease in hepatic production of ketones. They dismiss the first of these because there was no difference in the total ketonuria induced by any of the therapeutic procedures. The second they consider unlikely because no appreciable difference has been found between the rate of ketone utilization in the peripheral tissues of the normal dog and the rate observed in the diabetic hepatectomized dog (Chaikoff and Soskin, *Amer. J. Physiol.*, 1928, **87**, 58). They suggest, therefore, that inhibition of hepatic ketogenesis is the most likely explanation. The importance of insulin in inhibiting ketogenesis in diabetics is well known, and the more rapid recovery from ketosis following carbohydrate administration may be attributed to the increased utilization of sugar observed in these patients. The authors emphasize that the only disadvantage of early glucose therapy in the diabetic is the greater degree of hyperglycaemia, with its resultant intracellular dehydration, osmotic diuresis, and electrolyte loss. They claim that the judicious use of fructose can minimize these disadvantages and that administration of carbohydrate, in addition to adequate insulin and fluid, speeds recovery from diabetic ketosis. *J. Lister*

1364. **Nutritional Studies of Juvenile Diabetics Attending Summer Camp**
H. G. JACOBI. *Journal of Clinical Nutrition* [*J. clin. Nutr.*] **2**, 22–31, Jan.–Feb., 1954. 11 refs.

The height, weight, diet, and insulin requirements of 155 diabetic children attending a summer camp organized by the New York Diabetes Association have been studied. There were more children, both boys and girls, above average height than below. A tendency to underweight was noted in the boys, whereas two-thirds of the girls were distinctly overweight. An increase in the allowance of food was required by 32 out of 74 boys and 20 of 81 girls during their stay at the camp. At home about half the children were receiving a single daily dose of NPH insulin and most of the others a mixture of protamine zinc and ordinary insulin. For all the children the dose of insulin was reduced by 30% when they entered the camp. *K. O. Black*

1365. **The Effect of Hexamethonium Bromide on the Circulatory and Metabolic Response to Insulin Hypoglycemia in Man**
B. P. BILLINGTON, A. PATON, T. B. REYNOLDS, and S. SHERLOCK. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **43**, 880–887, June, 1954. 2 figs., 15 refs.

The Rheumatic Diseases

1366. **Nitrogen Mustard in Treatment of Systemic Lupus Erythematosus**

E. L. DUBOIS. *Archives of Internal Medicine* [*Arch. intern. Med.*] **93**, 667–672, May, 1954. 9 refs.

Following claims that nitrogen mustard is of value in the treatment of glomerulonephritis and also in that of systemic lupus erythematosus with renal involvement, the author studied the effect of this form of therapy and of treatment with triethylene melamine in 20 cases of the latter disease.

None of the patients was treated until the maximum possible benefit had been obtained with cortisone, and this steroid was administered throughout the trial. No improvement was noticed in 5 patients suffering from active disease without apparent renal involvement, nor in 4 with or without overt renal disease in whom there was established hypertension. Considerable improvement was observed, however, in the group of patients suffering from " nephrotic nephropathy ". The greater the degree of oedema and albuminuria, the greater was the response to treatment. All 20 patients were given nitrogen mustard intravenously in a single dose of 20 mg. in a dextrose infusion. In successful cases a diuresis occurred within 3 to 14 days. No serious toxic effects were observed.

Triethylene melamine was given to 5 of the patients in a total dose of 10 to 15 mg. over a 2- to 3-day period. In one of them agranulocytosis developed and in another a fatal aplastic anaemia. It was not used further because of its unpredictable behaviour in this disease.

Nigel Compston

ACUTE RHEUMATISM

1367. **Rheumatic Fever Prophylaxis. Control of Streptococcal Upper Respiratory Infection in Cardiac and Rheumatic Fever Patients and their Siblings; Preliminary Report**

R. A. TIDWELL. *Northwest Medicine* [*Northw. med. (Seattle)*] **53**, 470–476, May, 1954. 24 refs.

It is pointed out that long-continued administration of penicillin as a prophylactic against streptococcal infection of the upper respiratory tract is considered essential in the management of patients with cardiac disease or a history of rheumatic fever. All subjects with active infection are possible future victims of rheumatic fever, and since carriers of the streptococcus may endanger the health of contacts, family prophylaxis has been recommended.

At the out-patient clinic of the Children's Orthopedic Hospital, Seattle, a single daily dose of a slowly-excreted penicillin, " bicillin " (dibenzylethylendiamine dipenicillin G), was given by mouth to 57 children and 2 adults for periods ranging from 3 to 10 months. Of the 59 patients, 25 were ill at the beginning of the treatment, and among the remainder were 8 with congenital heart disease and 13 with a history of rheumatic fever. All the patients were given one tablet (containing 200,000 units) of bicillin daily. In spite of a fairly constant exposure to infection throat cultures examined monthly remained consistently negative for β-haemolytic streptococcus, except in 2 cases. There was no recurrence of rheumatic fever in the affected patients and no evidence of bacterial endocarditis in those with congenital or rheumatic heart disease. Time lost from school was reduced by over 80% compared with the time lost by the same group in the year preceding the start of prophylactic treatment. The author concludes that a single daily dose of bicillin is effective in eliminating the haemolytic streptococcus from the pharynx, and preventing a recurrence of rheumatic fever.

[No results are reported for a similar group not receiving penicillin prophylaxis. The efficacy of the drug in preventing recurrences of rheumatic fever is scarcely proven by these observations.]

Kenneth Stone

1368. **The Relation of the Serum Inhibitor of Serum-extracted Streptolysin S to Serum Phospholipid from the Standpoint of Rheumatic Fever**

A. D. WALLIS and E. VIERGIVER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 431–436, April, 1954. 1 fig., 13 refs.

There is a growing conviction that the haemolytic streptococcus is the cause of rheumatic fever, presumably acting through some antigen–antibody mechanism. An investigation was carried out at Pennsylvania Hospital, Philadelphia, to determine whether streptolysin S is the streptococcal component responsible for rheumatic fever. Serum from healthy subjects and from hospital patients, both children and adults [illness not specified], was analysed for its phospholipid content and for the inhibitor of streptolysin S, the method of Youngburg and Youngburg being used for estimation of phospholipid. Streptolysin S inhibitor was measured, normal human erythrocytes being used, against serum-extracted haemolysin contained in the supernatant of broth–serum cultures of a strain of streptococcus which produced streptolysin S but no streptolysin O. This supernatant, being unstable, was preserved at −16° C. or lyophilized, remaining potent at a titre up to 1:320 or 1:640 for at least 2 years. A haemolysin titration against a dilution of standard human serum and erythrocytes was made as a preliminary to each test in order to determine the combining dilution of haemolysin for each particular batch of erythrocytes.

The results showed that there was no real change with postprandial increase in serum phospholipid content; a low serum phospholipid level was found in association

with a very weak streptolysin S inhibitor, but with medium and high phospholipid levels the correlation was less definite.

Since it has been shown that the serum phospholipid level tends to be below normal in individuals who are susceptible to rheumatic fever, the authors consider that their findings lend support to the view that streptolysin S may be the cause of this disease, and that susceptibility to it may vary inversely with the strength of the natural serum inhibitor of streptolysin S. *E. G. L. Bywaters*

1369. **Heart Failure in Children with Active Rheumatic Carditis**

G. THOMAS. *British Medical Journal* [*Brit. med. J.*] **2**, 205–208, July 24, 1954. 3 figs., 7 refs.

In this paper from the Canadian Red Cross Memorial Hospital, Taplow, Bucks, it is suggested that in rheumatic carditis in children abnormal signs attributed to heart failure, which is less common than was formerly supposed, are in reality often due to pericardial effusion. Though the distinction may sometimes be difficult, it is well defined in the series of 30 cases here described.

Of these 30 cases, 23 in which pericardial effusion was diagnosed were all febrile at the onset—as often occurs early in a first attack. Common features included tachypnoea, chest pain, raised jugular venous pressure, abnormal signs at the lung bases, especially on the left side (usually due to pleural effusion), and leucocytosis. A high erythrocyte sedimentation rate and rapid changes in the heart size and shape as observed radiologically were invariable. The condition was found not to respond to digitalis. Although 4 of these 23 patients died, the prognosis is considered to be better than in cases of heart failure.

The other 7 patients, who had heart failure, were all afebrile. Failure occurred only in the presence of well-marked valvular lesions and cardiac enlargement, late in the disease or in second attacks. In all cases there were raised venous pressure and hepatic enlargement; 5 had rales at the lung bases, but none had pleural effusion; peripheral oedema and ascites both occurred in 2 cases. Increased body weight was observed only in the presence of peripheral oedema. There was no leucocytosis, but in all cases there was a low or sharply falling erythrocyte sedimentation rate. The heart size increased slightly in 3, but no rapid changes in size and shape were seen. Four cases responded well to digitalis, supplemented if necessary by low-sodium diet and mercurial diuretics; in the other 3 an initial response was succeeded by increased signs of failure and death in 2 to 6 weeks.

Details of 2 of the cases are presented to illustrate the differential features between the two conditions.

R. S. Stevens

1370. **An Evaluation of Large Doses of Cortisone in First Attacks of Rheumatic Carditis**

E. T. HEFFER, R. D. TURIN, S. R. SLATER, and I. G. KROOP. *Journal of Pediatrics* [*J. Pediat.*] **44**, 630–639, June, 1954. 17 refs.

The authors claim that early and intensive treatment with cortisone in doses adjusted to the individual case may prevent residual cardiac damage in first attacks of rheumatic carditis. In support of this claim they report the results in 19 cases in children aged between 5 and 15 years of age treated at the Jewish Hospital, Brooklyn, New York, all of whom were suffering from a first attack of rheumatic fever with carditis. The initial daily dose of cortisone was between 200 and 300 mg. divided in four oral doses. This was given for 2 weeks or longer until the disease process appeared to be suppressed, when the dose was reduced; the usual duration of treatment was 5 or 6 weeks. All the cases were carefully observed and blood counts and laboratory tests for rheumatic activity were carried out.

The authors were unable to find any residual cardiac damage in 13 of the children during an observation period varying from 6 to 14 months; all these 13 cases had been treated within the first 2 weeks of the illness. The remaining 6 patients, who were all treated later in the disease, had a systolic murmur at the end of the period of observation. Most of the patients showed a rebound phenomenon when the drug was stopped.

[The authors' conclusion that "our experience also indicates that cortisone in adequate dosage may be more effective in controlling carditis than salicylates" is hardly warranted, for there were no controls. The results achieved in this series appear to be very good, but they do not correspond with those achieved by others who have used the same treatment. The value of cortisone in the treatment of rheumatic fever can only be assessed by properly controlled studies.]

R. S. Illingworth

1371. **Incidence and Frequency of Infections at Specific Ages in Infancy and Childhood. With Special Reference to Upper Respiratory Infections in Potentially Rheumatic Susceptible Children**

N. EPSTEIN. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **87**, 600–606, May, 1954. 3 figs., 9 refs.

CHRONIC RHEUMATISM

1372. **The Intra-articular Injection of Hydrocortisone Acetate.** (Intra-articulaire toediening van hydrocortisonacetaat)

R. K. W. KUIPERS. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **98**, 1558–1561, June 5, 1954. 3 refs.

After discussing briefly the information that may be obtained by joint puncture and examination of the punctate as an aid to diagnosis in arthritic conditions, the author describes his experience in private practice with the intra-articular injection of hydrocortisone acetate. A dose of 25 mg. (or 10 mg. for the smaller joints) for 5 to 10 injections per case produced satisfactory results, as judged 4 weeks after completion of treatment, in 75% of 160 patients with various forms of rheumatic joint disease. Improvement was judged by lessening of the pain, stiffness, and inflammation, which was generally accompanied by simultaneous improvement in the condition of the punctate. The response was better in

osteoarthritic conditions (60% of patients improved) than in rheumatoid arthritis; in humeroscapular periarthritis, however, the results were generally inferior to those obtained by intravenous infusion of ACTH. The best results were seen in monarthritic conditions and in cases in which one or two joints in polyarthritis proved resistant to systemic treatment with gold or cortisone. The technique of injection of the joints presented no particular difficulties. *R. Crawford*

1373. **Oral Cortisone Therapy in Periarthritis of the Shoulder. A Controlled Trial**
N. J. BLOCKEY, J. K. WRIGHT, and J. H. KELLGREN. *British Medical Journal* [*Brit. med. J.*] **1**, 1455–1457, June 26, 1954. 6 refs.

At the Manchester Royal Infirmary the effect of cortisone was compared with that of an inert substance in treating 32 cases of periarthritis of the shoulder. The patients, all between 20 and 70 years of age, had periarthritis of one or both shoulders without radiological evidence of bone or joint disease and in all of them the erythrocyte sedimentation rate was normal; those with symptoms or signs of generalized arthritis were excluded. Half the patients were given a suspension of cortisone by mouth for 4 weeks and the other half received an inert suspension in the same amount, the latter being indistinguishable in both appearance and taste from the cortisone suspension.

All patients were instructed in shoulder exercises, and at the end of 4 weeks the shoulders of those who had not progressed satisfactorily were manipulated under general anaesthesia. At the end of the 4 weeks it was found that although some of the patients receiving cortisone had less pain before and after manipulation than the control group and fewer required restoration of movement under anaesthesia, some patients were not helped by the hormone. No statistical difference was observed between the results in the two groups.
Oswald Savage

1374. **Studies of the Serum Protein Fractions in Inflammatory Rheumatism.** (Études sur la répartition des protides sériques dans les rhumatismes inflammatoires. (Électrophorèse sur papier))
F. JACQUELINE, P. M. DE TRAVERSE, and L. BESSON. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **21**, 329–339, April, 1954. 41 refs.

The authors have determined, at the Institutes of Hydrology and Climatology of Paris and Aix-les-Bains, the serum protein levels in 97 cases of inflammatory rheumatism, comprising 62 cases of rheumatoid arthritis, 8 of Still's disease, 24 of ankylosing spondylitis, and 3 of gout. The serum protein level was below normal in only 8 of the cases, and was generally raised, being higher in men than in women. Except in cases of ankylosing spondylitis, in which the serum protein level was always raised, the degree of hyperproteinaemia was roughly proportional to the activity of the disease and to the erythrocyte sedimentation rate.

Paper electrophoresis of serum from patients with rheumatoid arthritis showed that the albumin fraction decreased and the globulin fraction increased as the disease became more active. Variations in the globulin fraction were found to be related to the type of arthritis. In early cases the alpha-2 globulin value was raised, whereas in more advanced cases showing fibrous or ankylosing changes the gamma globulin value also rose. The electrophoretogram in long-standing cases showed an increase in alpha-1 globulin if the disease was active, but this value was within normal limits in quiescent cases. The beta globulin value was slightly raised in one-fifth of cases. The changes in protein fractions in cases of Still's disease were similar to those in the adult type of rheumatoid arthritis. In the cases of ankylosing spondylitis the changes in the globulin fractions were less marked, and the authors believe this was associated with the less intense activity of the disease. In 2 of the 3 cases of gout there was a rise in gamma globulin level, but in the third case there was no change even during an acute attack.

They conclude that these findings are not specific for the diseases discussed, but may be of help in assessing prognosis and confirming the diagnosis of the type of lesion present. *F. Clifford Rose*

1375. **Osteitis Condensans Ilii and its Differentiation from Ankylosing Spondylitis**
M. THOMPSON. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **13**, 147–156, June, 1954. 8 figs., 21 refs.

After a comprehensive review of the literature relating to osteitis condensans ilii 20 cases seen at the Northern General Hospital and Royal Infirmary, Edinburgh, since 1950 are described, in which the initial *x*-ray examination revealed changes typical of this condition. The patients were females aged 26 to 47 years and all complained of low lumbar pain. In each case a full clinical, radiological, and pathological investigation was carried out.

In 7 cases the diagnosis was changed to that of ankylosing spondylitis because oblique views of the sacroiliac joints showed widening of the joint space and erosions. Later findings, such as a raised erythrocyte sedimentation rate and progressive limitation of spinal movements, lent support to this change in diagnosis. The differential diagnosis from ankylosing spondylitis proved difficult in 4 of the remaining cases, but in none of the 13 was there evidence of abnormality in the sacroiliac joint spaces. *X*-ray examination showed that the changes were predominantly unilateral in 6 cases. There was quite good correlation between the site of the pain and the site of sclerosis as seen radiologically.

Treatment consisted in a simple regimen of rest on a firm mattress, local application of heat, exercises, administration of an analgesic, and when necessary the use of a supporting belt. Only 2 patients failed to obtain substantial benefit.

The author considers that the findings suggest: (1) that there is a restricted or abortive type of ankylosing spondylitis which occurs especially in women, and (2) that osteitis condensans ilii is a definite clinical entity, accompanied by low back pain, and occurring predominantly in females. *B. E. W. Mace*

1376. **Ankylosing Spondylitis and Prolonged ACTH Therapy**
H. F. West and G. R. Newns. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **13**, 109–119, June, 1954. 8 figs., 5 refs.

In this paper from the Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases are reported the results in 6 cases of ankylosing spondylitis treated continuously for 1½ to 2 years with ACTH. The degree of adrenal stimulation was measured by the level and pattern of ketosteroid excretion, the authors pointing out that without such measurements it is impossible to assess the adrenal stimulus, and hence the amount of treatment, that is being given. The dosage of the hormone and the results of clinical and laboratory investigation in each case are well presented in charts, which the authors consider to show the impossibility of laying down a scheme of dosage even when a highly purified preparation of ACTH is being used.

In the first case the patient had been bed-ridden for some time on account of widespread ankylosis. Within 7 months of the beginning of treatment he was so much improved that he walked without aid. The erythrocyte sedimentation rate had fallen and bone density had returned almost to normal by the 9th month. Suspension of treatment for 2 days caused a febrile relapse. Eventually the dose of ACTH had to be reduced on account of hypertension. A second patient also showed improvement, but again the occurrence of hypertension interfered with treatment. The third patient felt improved and no advance of the disease occurred during treatment. Two other cases showed some benefit, while the last case probably did not improve. Raised blood pressure and a changed pattern of ketosteroid excretion were the main complications in this series.

The authors conclude that prolonged treatment with ACTH is justified only in really severe cases of ankylosing spondylitis in which *x*-ray therapy has not led to improvement. *G. Loewi*

1377 (*a*). **Tennis-elbow (Epicondylalgia Externa). Treatment with Hydrocortisone**
C. E. Quin and F. A. Binks. *Lancet* [*Lancet*] **2**, 221–223, July 31, 1954. 9 refs.

1377 (*b*). **Tennis-elbow Treated with Hydrocortisone Acetate**
A. H. G. Murley. *Lancet* [*Lancet*] **2**, 223–225, July 31, 1954. 13 refs.

1377 (*c*). **Hydrocortisone in Tennis-elbow**
D. E. Freeland and M. de G. Gribble. *Lancet* [*Lancet*] **2**, 225, July 31, 1954. 5 refs.

The work described in these three papers was aimed at assessing the value of hydrocortisone in the treatment of the condition known as tennis elbow. There are numerous references to the literature concerning the histopathology of the syndrome, and some emphasis is laid upon the ineffectiveness of the many methods of treatment hitherto employed, with the single exception of surgery, which, though effective, is a rather major undertaking for a relatively minor complaint that in any case spontaneously recovers in due course. Quin and Binks present the results in 31 cases, with much clinical information. They were not convinced that trauma was a significant aetiological factor, and were impressed with the fact that there was often a history of "aches and pains in other parts of the body", suggesting that the condition is a manifestation of a more generalized disturbance. Pain is aggravated by gripping and dorsiflexion of the wrist. Murley notes that the condition commonly affects those over 30 years of age who undertake unaccustomed activities involving repeated pronation and supination while the hand is gripping.

The authors of all three papers compare the effect of hydrocortisone with that of procaine, another commonly used method of treatment. Quin and Binks injected procaine at the maximum point of tenderness and then injected varying amounts of hydrocortisone into the identical spot. The authors of the other two papers injected 25 mg. of hydrocortisone alone into the area of maximum tenderness; or, in their control series, 1 ml. of 2% or 5% procaine respectively. Results were assessed at definite intervals afterwards. Quin and Binks recorded 26 successful results from a single injection (combined procaine and hydrocortisone). Of the 5 cases in which this treatment was a failure, 2 responded after a second injection. Various reactions are described. Murley records 14 successful results and 5 failures out of 19 cases. Subsequent relapses were common, but responded to further injections; no patient was made worse. Of the 18 patients treated with procaine alone as a control "a few found their symptoms improved but most were unrelieved". Freeland and Gribble, on the basis of 16 injections in 14 cases, conclude that "the local injection of hydrocortisone . . . was no more or less effective in curing tennis-elbow than a similar injection of 5% procaine". They express surprise that procaine, being only a short-lasting local analgesic, produced such a clear and long-lasting improvement at all. [Such a view overlooks the other pharmacological actions of this substance. There is perhaps some doubt about the advisability of using procaine as a control injection in such cases as these, as it is known to have some degree of effectiveness in the treatment of this condition.]

The only deduction to be made from consideration of the three papers together is that Freeman and Gribble obtained equally effective results from hydrocortisone and 5% procaine, while Murley, using only 2% procaine, failed to observe any effective response in the patients so treated, which seems to indicate that procaine may be as effective as hydrocortisone provided it is used in sufficient concentration. *Harry Coke*

1378. **Osteoarthritis and Rest**
F. D. Hart, M. Watkins, D. Burley, and M. T. Richards. *British Medical Journal* [*Brit. med. J.*] **2**, 269–271, July 31, 1954. 11 refs.

The authors point out that in articles and textbooks dealing with the treatment of osteoarthritis the value of rest is nearly always emphasized but its hazards are rarely mentioned. They agree that excessive use of an affected joint will produce a sharp reaction within 24 to 48 hours, but hold that immobilization may produce much more prolonged disability. When elderly patients

are rested in bed as part of the treatment of cardiac decompensation, bronchitis, pneumonia, bleeding peptic ulcer, or other diseases, they may develop for the first time joint symptoms associated with osteoarthritis, or existing symptoms of osteoarthritis of the hips or knees may be severely aggravated. The histories of 4 such patients admitted to St. Stephen's Hospital, London, are described to illustrate this point.

Harrison *et al.* (*J. Bone Jt Surg.*, 1953, **35B**, 598) have emphasized " the necessity for use and compression of cartilage in order to maintain its continued health ", while Lloyd-Roberts (*J. Bone Jt Surg.*, 1953, **35B**, 627) has pointed out the effect of fibrosis and shortening of the capsule in the production of symptoms in osteoarthritis of the hip. Those two findings together help to explain the deterioration which occurs in a patient's weight-bearing joints during a period of complete rest in bed, when there is a tendency for the hip to be held in flexion and lateral rotation, while the knee is also flexed. In order to prevent the adverse changes which follow long-continued maintenance of this position the authors suggest that patients should spend part of the day lying flat, and selected patients with flexion deformities already present should be induced to spend periods in the prone position. Exercise of the hips, knees, and ankles should be undertaken as soon as possible. Analgesics should be used freely if pain prevents proper cooperation in the performance of these exercises, while the injection of a local analgesic into ligamentous attachments or the intra-articular injection of hydrocortisone may be useful in helping to mobilize stiff and painful knees. *C. E. Quin*

1379. **A Comparison of Cortisone and Aspirin in the Treatment of Early Cases of Rheumatoid Arthritis**
MEDICAL RESEARCH COUNCIL/NUFFIELD FOUNDATION JOINT COMMITTEE ON CORTISONE, ACTH, AND OTHER THERAPEUTIC MEASURES IN CHRONIC RHEUMATIC DISEASES. *British Medical Journal* [*Brit. med. J.*] 1, 1223–1227, May 29, 1954. 4 refs.

In an investigation carried out at six centres in England and Scotland 61 patients suffering from rheumatoid arthritis who had all developed the disease not more than 9 or less than 3 months previously were treated at random with adequate doses of either cortisone or aspirin. The patients were admitted to hospital for a minimum of 4 weeks, when treatment was initiated. Those treated with cortisone, which was labelled " Tab. (or Mist.) Rheumatic A " and given by mouth, received 300 mg. on the first day; the dose was gradually reduced until the 3rd week, after which " the minimum dosage that would restore maximal functional efficiency without producing serious side-effects " was employed. Patients given aspirin, which was labelled " Tab. Rheumatic C ", were started on 6 g. daily, and this too was cut down to a minimum satisfactory dose when possible. At the 12th week drug treatment was gradually withdrawn, and during the 13th week no cortisone or aspirin was given and the patients were observed and investigated. If symptoms recurred the 12 weeks' course of the standard dose was resumed.

Patients were assessed before and at regular intervals during treatment, the assessment including judgment of the patient's functional capacity and of the activity of the disease. Strength of grip, dexterity, joint tenderness, and range of movement were also assessed. Complications, side-effects, and further involvement of new joints were noted and haemoglobin value and erythrocyte sedimentation rate regularly estimated.

Of the 61 patients originally admitted to the trial 3 who were being treated with aspirin defaulted, and 2 of these cases were regarded as failures of treatment. Of the remaining 58 patients, 30 received cortisone and 28 aspirin. At the end of a year the results were analysed, and it was found that as regards joint tenderness both treatments had had equal effects. The results in regard to range of movement and strength of grip showed that both treatments were about equal in producing an increase of 20 to 30% in range of movement and one of 40 to 50% in strength of grip. Similarly both treatment groups showed equal inprovement in dexterity, but in respect of haemoglobin level and erythrocyte sedimentation rate there was a significantly greater improvement in the group treated with cortisone. Clinical assessment showed a remarkable similarity between the two treatment groups; minor complications of treatment were also equally distributed between the two groups.

It is envisaged that the trial will continue into a second and third year.

[It is important to realize that this investigation covers only one aspect of the comparison between the efficacy of cortisone and of aspirin in rheumatoid arthritis. The study was not of a wide series of patients suffering from rheumatoid arthritis at all stages, but was confined to a small group of sufferers in the early stages of the disease.] *W. Tegner*

1380. **The Treatment of Rheumatoid Arthritis with Multi-articular Local Injections of Hydrocortisone Acetate.** (Traitement de la polyarthrite chronique évolutive par les injections locales multi-articulaires d'acétate d'hydrocortisone)
R. WEISMANN-NETTER, R. LÉVY, and P. LORCH. *Presse médicale* [*Presse méd.*] **62**, 852–855, June 2, 1954. 1 ref.

The authors, working at the Hôpital Beaujon, Paris, treat rheumatoid arthritis by multiple intra-articular injections of hydrocortisone acetate under general anaesthesia. Depending on the size of the joint, 10 to 100 mg. of hydrocortisone is injected into each of the affected joints at one session. The total dose of several hundred mg. given has not produced any of the side-effects associated with systemic therapy with adrenal hormones. Depending on the result, the treatment may be repeated two or three times at weekly intervals; there has been no apparent loss of effect with repeated injections, and improvement has been maintained for periods varying from a few weeks to several months. The authors prefer this method to daily injections of two or three joints under local analgesia as it saves time and is considered to be less disagreeable to the patient.

Of 7 cases of advanced rheumatoid arthritis treated by this method after failure to respond to other therapy,

including administration of cortisone and ACTH, 3 showed marked improvement, 3 were moderately improved, and one did not respond; the cause of failure in this last case was considered to be insufficient dosage. In view of the absence of side-effects and the encouraging results obtained, the authors consider this to be one of the best methods of treatment of rheumatoid arthritis so far available.

[Seven cases is too small a series upon which to base any assumption, but further work is continuing.]

F. Clifford Rose

1381. **Cortisone Acetate *v.* Cortisol in the Treatment of Rheumatoid Disease**
H. F. West and G. R. Newns. *Lancet* [*Lancet*] **2**, 168–169, July 24, 1954.

The authors have compared the effects of cortisone acetate and of cortisol (hydrocortisone " free alcohol ") in 22 cases of rheumatoid arthritis under treatment at the Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases. These patients, who had previously received a long-term programme of cortisone acetate treatment, were transferred to cortisol treatment and observed for 3 months. The results were assessed on the basis of physical ability, strength of grip, and erythrocyte sedimentation rate. The authors conclude that cortisol is more potent as an antirheumatic agent than cortisone acetate, but that on the other hand it is more prone to produce undesirable side-effects.

Oswald Savage

1382. **The Haemagglutinating Factor in Rheumatoid Arthritis.** (Den hämagglutinerande faktorn vid rheumatoid arthrit)
N. Svartz and K. Schlossmann. *Nordisk Medicin* [*Nord. Med.*] **51**, 668–669, May 13, 1954. 5 refs.

In a further investigation carried out at the Karolinska Hospital, Stockholm, of the factor present in the serum of patients with rheumatoid arthritis which agglutinates sensitized sheep erythrocytes, inactivated serum was treated with sheep cells to remove heterophile antibody, diluted with 14 volumes of water, and kept at 4° C. for 48 hours; the precipitate which formed was separated by centrifugation and redissolved in saline. This solution was found to contain a haemagglutinin for sensitized sheep erythrocytes which was specific to serum from rheumatoid arthritic patients. A factor with similar properties could be produced *in vitro* by growing bacteria isolated from the throat of patients with rheumatoid arthritis on a medium containing bovine or human collagen tissue.

D. J. Bauer

1383. **Effect of Post-partum Plasma in Rheumatoid Arthritis**
D. H. Neustadt, J. Geiger, and O. Steinbrocker. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **13**, 131–135, June, 1954. 21 refs.

A pilot study to determine the clinical effects of transfusion of post-partum plasma was carried out at the Lenox Hill Hospital and the Hospital for Joint Diseases, New York. For this purpose 11 patients suffering from active rheumatoid arthritis of 6 months' to 15 years' duration were given post-partum plasma by intravenous injection, each patient receiving about 250 ml. weekly for 10 weeks. The effects were assessed weekly by two observers on the basis of four subjective factors—namely, pain, stiffness, sense of well-being, and joint tenderness; in addition, laboratory investigations, including estimation of haemoglobin content and erythrocyte sedimentation rate, were carried out fortnightly. The study, however, failed to demonstrate any consistent subjective or objective improvement from this form of treatment.

G. Loewi

1384. **Shoulder Affections in Rheumatoid Arthritis**
V. A. I. Laine, K. J. Vainio, and K. Pekanmäki. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **13**, 157–160, June, 1954. 2 figs., 6 refs.

The incidence of involvement of the shoulder in cases of rheumatoid arthritis was studied at the Rheumatism Foundation Hospital, Heinola, Finland. Of 277 patients with proven rheumatoid arthritis, 159 had shoulder symptoms, and these were investigated in detail. A variety of disorders was found, two or more of these often occurring in the same patient.

The commonest affection was a rheumatoid condition of the scapulo-humeral joint (75 cases), but arthritis of the acromio-clavicular and sterno-clavicular joints, tendinitis and tenosynovitis around the shoulder-joint, and subacromial bursitis were also noted. The next most frequent affection, however, was the " scapulocostal syndrome ", characterized by pain mostly localized in the upper scapular area but sometimes radiating, with muscular " trigger-points ", which was found in 55 cases. The authors state that this last condition is relieved by anaesthesia of the trigger-points, and that such treatment often affords welcome relief to the arthritic patient.

Other non-rheumatoid conditions, such as periarthritis, osteoarthritis, radicular pain, and sympathetic reflex dystrophy, were found in a few cases.

B. E. W. Mace

1385. **How to Prevent Crippling in Rheumatoid Arthritis**
M. Kelly. *Lancet* [*Lancet*] **1**, 1158–1161, June 5, 1954. 5 figs., 12 refs.

Methods of preventing or correcting deformities due to rheumatoid polyarthritis, so that the patient does not become fixed in an armchair posture, are discussed. Flexion of the knee should be prevented by application of a weight-bearing caliper, by quadriceps exercises, and by daily walking. If necessary the joint is manipulated under anaesthesia, the aim being to straighten the knee and to keep the patient walking. As regards hand deformities, a small hand plaster to immobilize only the metacarpo-phalangeal joints is recommended. For inflamed wrist-joints a wrist plaster which allows free finger movements is advocated. It is stated that ankylosis does not develop with this method of treatment.

In the author's view it is a mistake to move a painful joint through a full range of movements daily; moreover, immobilization of a joint for a few weeks does not result in ankylosis. The patient should walk each day and should not be allowed to become bed-ridden.

J. B. Millard

Physical Medicine

1386. **Effect of Ultrasonic Energy on Blood Flow**
C. J. IMIG, B. F. RANDALL, and H. M. HINES. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] **33**, 100–102, April, 1954. 4 refs.

In experiments performed at the State University of Iowa the effects of the application of ultrasonic energy to the hind legs of anaesthetized dogs on the tissue temperature and blood flow were studied. The blood flow through the femoral artery was measured before and during treatment by means of an electromagnetic flow meter, and subcutaneous and muscle temperatures were recorded by means of an iron–constantan thermocouple needle. With a treatment unit generating vibrations at 800,000 c.p.s. and a mineral-oil coupling medium, a water-cooled applicator 10 sq. cm. in area was applied to the skin over the gastrocnemius muscle " with massage-like movements ". Two outputs were used, 0·5 watt per sq. cm. and 1·20 watt per sq. cm., each for a period of 15 minutes.

The lower dosage did not affect the blood flow, although the muscle temperature was increased to an average level of 37·2° C. and that of the subcutaneous tissue on the opposite side of the limb to 39·3° C. The higher dosage caused an increased blood flow in the muscle and a rise in the temperature of muscle to an average of 41·9° C. and of the subcutaneous tissue on the opposite side to 43·4° C. Owing to the water-cooling of the applicator the temperature of the tissue immediately under it did not rise. The authors state that the efficacy of ultrasonic energy in increasing muscle blood flow was related to the degree of hyperthermia produced, but that no increase in flow occurred until the muscle temperature reached 42° C. They noted tissue coagulation in several cases. *J. B. Millard*

1387. **Effect of Microwave-induced Heating on the Blood Flow through Peripheral Skeletal Muscles**
A. W. RICHARDSON. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] **33**, 103–107, April, 1954. 1 fig., 13 refs.

Studies of the effect of microwave irradiation on the muscle blood flow in anaesthetized dogs are reported from Indiana University. The cutaneous and subcutaneous tissues of the hind limb were removed, the vascular supply of the foot was occluded, and the limb encased in paraffin wax. Blood flow from the gastrocnemius muscle was measured by means of an electromagnetic flow meter and the muscle temperature recorded before, during, and after irradiation of the limb, a commercial 12·25-cm. microwave generator being used at an output of 63 watts for a period of 15 minutes.

There was a steady rise in muscle temperature during the treatment period to an average maximum of 46° C., and an average increase of 85% in the blood flow. The increase in blood flow did not start until the muscle temperature had reached 44° C., and reached its peak several minutes after cessation of heating. This confirms previous observations by the author and others that a critical temperature must be surpassed in order to increase the blood flow in muscle, and it is suggested that this may be a factor of significance in clinical microwave therapy. *J. B. Millard*

1388. **Echographic Visualization of Lesions of the Living Intact Human Breast**
J. J. WILD and J. M. REID. *Cancer Research* [*Cancer Res.*] **14**, 277–283, May, 1954. 13 figs., 18 refs.

In this paper is described an investigation at the University of Minnesota of the use of ultrasonic techniques in determining the histological structure of tissues. For this purpose the breast was chosen, but only because it is a conveniently accessible organ and as a first step toward the examination of less accessible sites, such as the gastrointestinal tract, cervix uteri, or prostate, with a view to the early detection of neoplasms.

For the examination of biological tissues by means of ultrasonic echoes the term " echography " has been suggested. The principle of the echograph is that an electronic clock initiates bursts of sound energy which are traced on a cathode-ray tube. A transmitter receives these pulses and excites a piezoelectrical crystal to produce a narrow beam of sound energy. The sound beam is applied to the tissues via a water column. The echoes returning from the tissues are received by the same crystal and are amplified to deflect the trace on the cathode-ray tube. This pattern is called the echogram. By comparing the echogram obtained from one breast with that from the opposite breast it is possible to detect an abnormal pattern if a tumour is present, by virtue of the altered reflection of the sound beam. The nature of the lesion can be postulated, as malignant tumours return more sound, and non-malignant tumours less sound, than normal tissue. Thus if, on calculating the area under the echogram and comparing it with the echogram of the normal breast, the area ratio of the tumour echogram to the control echogram is found to be less than 1, the lesion is non-malignant; if greater than 1, then it is malignant. These findings have been confirmed by pathological examination.

An alternative method of presenting the information is by recording the echo signals as spots of light on the echogram, the intensity varying with the signal returned from the tissues. This method has the advantage that the beam can be moved to successive points and a series of echograms obtained to demonstrate the lesion in two dimensions. A malignant tumour appears as a bright area and a non-malignant tumour as a dark area when compared with the intensity from normal tissue at the same depth.

Several cases are described, with photographs of the apparatus and some echograms. *J. B. Millard*

Neurology and Neurosurgery

1389. **Photo-metrazol Activation in Children**
M. W. LAUFER, E. DENHOFF, and E. Z. RUBIN. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **6**, 1–8, Feb., 1954. 3 refs.

The photo-leptazol test devised and described by Gastaut (*Electroenceph. clin. Neurophysiol.*, 1950, **2**, 249; *Abstracts of World Medicine*, 1951, **9**, 309) which is claimed to provide " a new means of evaluating the existence of an organic or functional change in the diencephalon " was carried out at the Emma Pendleton Bradley Home, Riverside, Rhode Island, on 31 children aged between 6 and 12 years. In 10 cases it was repeated and found to give similar results on each occasion. In order to make the test applicable to younger children an attempt was made to perform it during induced sleep, but the hypnotic agents used abolished the photo-leptazol response. The patients suffered from various psychiatric disorders, which are classified by the authors as organic and non-organic, the former including epilepsy and the " organic syndrome of behavior " [but not apparently including anything within the commonly accepted meaning of the term "organic "].

Gastaut's " polyspike " was never seen and the response taken as threshold is described as a " spike wave burst ". While the range of thresholds was the same in each case, namely, 1·8 to 8·1 mg. of leptazol per kg. body weight, the mean in the " organic " group was 4·31 mg. and in the inorganic 6·54 mg. per kg. Tentative thresholds are suggested: for the normal, 6·5 mg. or over, and for the abnormal, 5·1 mg. or below [but there is nothing in the paper which makes these figures acceptable to the reader]. *W. A. Cobb*

1390. **The Metrazol-flicker Threshold in Neuro-psychiatric Patients**
D. M. LEIBERMAN, J. HOENIG, and M. HACKER. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **6**, 9–18, Feb., 1954. 4 figs.

Using a technique slightly modified from that of Gastaut [see Abstract 1389] the authors have reassessed the value of the photo-leptazol test in 124 neuropsychiatric cases of various types seen at the Bethlem Royal and Maudsley Hospitals, London.

Unlike Gastaut they did not find a constant type of response, that is, the frontal " polyspikes " associated with jerks in flexion of the limbs and trunk as described by him, but rather a variety of combinations of spikes with slow waves. The mean threshold for all cases was found to be 6·0 mg. of leptazol per kg. body weight; in cases of idiopathic epilepsy (4·4 mg. per kg.) and catatonic schizophrenia (4·0 mg. per kg.) it was lower, though not for schizophrenic patients as a group.

These findings are similar to those of Gastaut, but the low threshold in hysterical subjects which he reported was not confirmed. No agreement was found between threshold and body weight, possibly because the leptazol did not have time to diffuse throughout the body as a whole. The authors conclude that the photo-leptazol test has little diagnostic value, but might be used to estimate the tendency of various neuronal systems to discharge. *W. A. Cobb*

1391. **Activation of the Electroencephalogram with Chloralose.** (L'activation des électroencéphalogrammes par le chloralose)
G. VERDEAUX, J. VERDEAUX, and R. MARTY. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **6**, 19–28, Feb., 1954. 6 figs., bibliography.

The authors report from the Hôpital Sainte-Anne, Paris, the effect of chloralose as an " activator " of the electroencephalogram (EEG). The drug was administered to 245 adult patients, the dose usually being 0·5 g. by mouth, either alone or along with 0·5 mg. of scopolamine. EEGs were recorded before and several times during the 2 hours after the ingestion of the drug.

Just over half the patients (124) presented with unconfirmed attacks of uncertain origin or with disturbances of character or behaviour, but without true fits. Among these the EEG was unchanged in 51 cases and " activated " in 73; this activation consisted in " hypersynchrony " in most cases, spikes being recorded in only 2 cases. The other 121 patients had epileptic attacks, and among these the EEG remained unchanged in 32 cases. Of the remainder some showed only hypersynchrony, but in the majority there were spikes or spike-and-wave complexes, which were particularly marked among the patients with petit mal. The clinical effects of the drug were generally insignificant, though in 10 epileptic patients grand mal attacks were provoked.

These results are discussed in relation to the considerable experimental evidence already published regarding the effect of chloralose on the EEG. The test is advocated for the study of " certain psychic forms of epilepsy " and especially for the diagnosis of petit mal. *W. A. Cobb*

1392. **The Electroencephalogram in Pernicious Anaemia and Subacute Combined Degeneration of the Cord**
J. N. WALTON, L. G. KILOH, J. W. OSSELTON, and J. FARRALL. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **6**, 45–64, Feb., 1954. 9 figs., 11 refs.

At the Royal Victoria Infirmary, Newcastle upon Tyne, the authors have recorded the electroencephalogram (EEG), before and after treatment, of 80 relapsed patients with pernicious anaemia of whom 56 had only slight or no neurological involvement and 24 had subacute combined degeneration of the cord. In the former group the EEG before treatment was abnormal in 4 cases

with mental disturbance and also in 31 (60%) of the remaining 52 cases. Improvement in the anaemia usually began within 10 days of starting treatment with vitamin B_{12} (cyanocobalamin) and the EEG became normal in the majority of cases. In 10 cases previously classed as normal there was a significant increase in frequency of the alpha rhythm after treatment.

Of a further 50 patients first examined electroencephalographically after treatment had been in progress for periods between 3 months and 8 years (average 18 months), the EEG was normal in 38 cases, and 4 more showed improvement as treatment continued. In only one case among 10 patients suffering from other forms of anaemia was there significant abnormality in the EEG, and this was attributed to coincident hypertension.

The authors suggest that the high incidence of EEG abnormality in untreated cases of pernicious anaemia is due not to the anaemia *per se*, but to a specific metabolic defect, possibly some alteration in glucose and pyruvate metabolism. *W. A. Cobb*

1393. **Electroencephalographic Findings in Intracranial, Arterial and Arterio-venous Aneurysms and Subarachnoid Haemorrhages.** [In English]
J. HUSBY, G. NORLÉN, and I. PETERSÉN. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. neurol. scand.*] **28**, 387–400, 1954. 3 figs., 12 refs.

Electroencephalographic studies have been made at the Serafinerlasarett, Stockholm, on 94 patients with proved or suspected intracranial aneurysms, some of which were multiple and some bilateral. There were 39 cases of arterial aneurysm, 38 cases in which there had been subarachnoid haemorrhage without proof of aneurysm, and 17 of arterio-venous aneurysm. Of the 77 cases of arterial aneurysm and of subarachnoid haemorrhage without aneurysm, 38 had focal or lateralizing activity and in 20 the electroencephalogram was normal. It was often possible to lateralize the aneurysm, and localizing activity was chiefly found with aneurysms arising from the middle cerebral artery. Patients with arterio-venous aneurysms showed an abnormal electroencephalogram, usually with focal or lateralizing activity. [This paper is of academic interest, but has not much clinical application.] *Hugh Garland*

1394. **Laminar Cortical Blocking and its Relation to Episodic Aggressive Outbursts**
C. GROSSMAN. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **71**, 576–587, May, 1954. 6 figs., 18 refs.

The author reports his observations at the Veterans Administration Hospital, Boston, on an abnormal response evoked by auditory stimulation during sleep in patients with episodic psychopathic behaviour. The normal electroencephalographic change in response to an auditory stimulus during sleep in man is a slow biphasic wave followed by a train of waves at 14 cycles per second. The amplitude of both components may be reduced in an area where there is a gross lesion. By contrast, in patients showing episodic rage or aggressiveness, only the faster component may be changed, its negative phases being reduced and its positive phases increased and spike-like; there are sometimes also waves at 6 to 7 cycles per second, both being best seen in the posterior parieto-temporal regions.

In experiments on cats under diallyl barbituric acid (" dial ") narcosis he found that in this animal bursts (" spindles ") are modified by application to the cortex of filter paper soaked in 2% cocaine solution and also during the passage of " spreading depression ", the change consisting in loss of the negative phases and accentuation of the positive phases.

It is suggested that the " 6 and 14 per second positive spikes " of Gibbs and Gibbs (*Neurology*, 1951, **1**, 136) are modified sleep spindles and are not particularly associated with epilepsy. Such clinical manifestations as rage may be due to loss of cortical control due to blocking of the superficial layers of the cortex in an association area. *W. A. Cobb*

1395. ***Listeria monocytogenes* Meningitis. Summation of Literature and Report of Two New Cases**
S. M. FINEGOLD, J. G. BRADLEY, M. K. CAMPBELL, and A. J. GREENBERG. *Archives of Internal Medicine* [*Arch. intern. Med.*] **93**, 515–527, April, 1954. 34 refs.

The authors briefly review the 37 cases of meningitis due to *Listeria monocytogenes* reported in the literature and describe 2 further cases seen by them at the Minneapolis General Hospital.

In this type of meningitis the clinical picture is not distinctive, the patient usually presenting with an acute suppurative meningitis, although chest symptoms may be prominent in the initial period of infection. The first specimen of cerebrospinal fluid obtained often shows a predominance of polymorphonuclear leucocytes. Final identification of the organism, morphologically resembling a diphtheroid, depends on the production of keratoconjunctivitis in the rabbit by gently swabbing a broth culture on the tarsal conjunctiva without breaking the mucosal surface. This test gave a positive reaction with the organism isolated from the 2 cases now reported.

The authors also carried out sensitivity studies on 6 strains of *Listeria monocytogenes* from cases in human beings. From the results of these tests, and on the basis of the successful treatment of their own 2 cases, they consider the administration of chlortetracycline (aureomycin) or oxytetracycline (" terramycin ") in conjunction with sulphadiazine and/or streptomycin to be the most effective method of treatment.

E. C. Hutchinson

1396. **Optic Neuritis in Relation to Demyelinating Diseases. A Clinical Study**
A. SCHLOSSMAN and C. C. PHILLIPS. *American Journal of Ophthalmology* [*Amer. J. Ophthal.*] **37**, 487–494, April, 1954. 11 refs.

Of the 72 cases of optic neuritis reviewed, 83·3% were retrobulbar; 69·4% of the patients with optic neuritis had multiple sclerosis. Visual disturbance was the initial symptom in 17 cases. In 19 cases the first attack of optic-nerve involvement occurred after a diagnosis of multiple sclerosis had been established by other means.

Seven patients gave a history of gradual loss of vision, while 10 patients did not give a history of any visual loss. In 10 cases there were no known recurrences; it is possible that many recurrences remain undetected. In only 7 cases was edema of the nerve head observed. Nevertheless, secondary optic atrophy is more frequently noted than is primary. Recovery is often incomplete and some tell-tale evidence often remains in the visual field. . . . The pathologic involvement is usually more extensive than one would expect from the clinical manifestations alone.—[From the authors' summary.]

1397. **The Relationship of Retrobulbar Neuritis to Multiple Sclerosis**

R. G. TAUB and C. W. RUCKER. *American Journal of Ophthalmology* [*Amer. J. Ophthal.*] **37**, 494–497, April, 1954. 3 figs.

Of 87 patients followed for 10 to 15 years after an initial bout of acute retrobulbar neuritis, 28 (32·2%) developed evidence of multiple sclerosis. Twenty-six were in the age group 20 to 44 years at the time of the initial bout. The authors' data suggest that an individual of this age group who has an attack of acute retrobulbar neuritis has a 40 to 50% chance of having multiple sclerosis within 10 to 15 years. In the cases in which retrobulbar neuritis occurs before the age of 20 years, the chance of multiple sclerosis appearing is less likely, and when it occurs after the age of 44 years the chance is remote.—[From the authors' summary.]

1398. **Prevalence of Disseminated Sclerosis in Northern Ireland**

R. S. ALLISON and J. H. D. MILLAR. *Ulster Medical Journal* [*Ulster med. J.*] **23**, Suppl. 2, 5–27, March, 1954. 2 figs., 31 refs.

A survey, covering the 3-year period from October, 1948, to October, 1951, was carried out by the authors (from the Royal Victoria Hospital, Belfast) in an attempt to obtain precise information on the prevalence, incidence, and geographical distribution of disseminated sclerosis in Northern Ireland. Previously, the only figures available were those obtained from records of mortality and hospital attendances.

Cases were divided into the following categories. (1) Early cases, in which there were few or no physical signs, but a recent history of remitting symptoms of the kind commonly associated with the disease, such as transitory uniocular blindness, double vision and vertigo, paraesthesiae, and numbness or weakness in one or other of the limbs. (2) Probable cases, in which there was no reasonable doubt about the diagnosis and which showed not only remitting symptoms, but also some physical disablement and the presence of physical signs explicable only on the basis of multiple lesions. (3) Possible cases, in which the findings were suggestive of the disease—and no other cause for them could be found—but where the history was progressive or static and there was insufficient evidence of scattered lesions at different levels of the nervous system. And lastly, (4) discarded cases, that is, cases in which sooner or later the existence of some other disease became apparent and the diagnosis of disseminated sclerosis had to be abandoned.

The prevalence rate of the disease was defined as the number of cases in Groups 1, 2, and 3 per 100,000 of the population aged over 20. Over the 3-year period the number of notifications was 887, of which 187 were subsequently rejected as discarded cases. Of the remainder, 79 were early cases, 476 probable cases, and 145 possible cases, and of the total 700 patients, 310 were men and 390 women. Since the 1951 census showed the total population of Northern Ireland to be 1,370,709, the prevalence rate was calculated to be 79 per 100,000 persons over 20. The fact that this figure is higher than comparable figures for other European countries and the U.S.A. and Canada does not necessarily mean that the disease is significantly more prevalent in Northern Ireland than in those countries, since there is great lack of uniformity in the criteria taken for the acceptance of cases, and also the differences in the age and sex distributions of the different populations must be taken into account. The evidence does, however, confirm the previous impression that Northern Ireland had a high prevalence rate.

The incidence rate was defined as the number of new cases occurring each year per 100,000 of the population. The figure obtained for all the diagnostic and age groups was 2·74 (males 2·56, females 2·91). If only "probable" cases were included, the figure became 1·61 (males 1·43, females 1·78) per 100,000. For various reasons these figures may well be an underestimate. The figure of 2·74, however, is not very different from that for the incidence rate in Winnipeg (2·23), but is higher than that for New Orleans (0·83). Again, age and sex differences of the populations may effect the comparison. In this survey, the incidence rates were low during adolescence, increased to a maximum for the age-group 30–39 years, and then fell again. In general, the rate among females exceeded that among males. There was no evidence to suggest that disseminated sclerosis was more prevalent in any one region of Northern Ireland than in another, nor was there any tendency to focal distribution of cases.

Adrian V. Adams

1399. **Familial Incidence of Disseminated Sclerosis in Northern Ireland**

J. H. D. MILLAR and R. S. ALLISON. *Ulster Medical Journal* [*Ulster med. J.*] **23**, Suppl. 2, 29–91, March, 1954. 45 figs., 41 refs.

As part of the survey of the prevalence of disseminated sclerosis in Northern Ireland [see Abstract 1398] the authors investigated the familial incidence of the disease. Of 668 families investigated, 2 or more members were affected in 44, giving an incidence of 6·58%. In each of these families the propositus (that is, the case which brought the family under investigation) was personally examined. In 23 families 2 or more cases were personally examined and in 6 further families in which only the propositus could be examined the evidence from other sources was sufficiently strong to warrant a firm diagnosis in other members; in 15 families the evidence as to the second or other members was less certain, being based mainly on documentary evidence. In addi-

tion, the incidence of other neurological conditions found in near relatives was recorded. This group might well have contained further cases of disseminated sclerosis, but it was not used in the calculation of familial incidence.

If it be assumed that the disease is the expression, precipitated by environmental factors, of a specific genotype, then it may be expected that the same genotype will occur more frequently in the sibs of affected persons than in the general population. Thus, after excluding the propositi from the calculations, all other sibs have independently the same chance of being affected. The figure obtained by dividing the number of affected sibs by the total number of sibs will then give the incidence in the sibs, which can be compared with that for the general population. When all age and diagnostic groups were included the incidence in the sibs of the propositi was 1·15%, compared with 0·072% for the general population. If only the " probable " cases were included, the incidence in the sibs was 0·66%, compared with 0·05% for the general population.

It was thus estimated that the incidence in the sibs of the propositi was between 5 and 15 times as great as the prevalence rate in the general population. It is emphasized that, although these figures are impressive, it is difficult to be certain that they are statistically significant because of the difficulties in determining the size of the sampling error involved and in making corrections for age. *Adrian V. Adams*

Radiological examination revealed changes in the intervertebral disk spaces in 7 cases, " arthrosis " also in 7, and anomalies of the lumbo-sacral junction in 4 cases, more than one of these abnormalities being present in certain cases. Lumbar puncture, performed in 11 instances, showed abnormality of the cerebrospinal fluid as manifested by increased number of cells and a raised protein content, in only 2 cases.

Surgical exploration was carried out in 11 cases, in 2 of which definite herniation of a disk was found and bony projections into the space in a further 2. In 3 other cases epidural venous dilatation was observed; the remaining 4 were entirely normal. The authors were able to follow up 15 patients for periods up to 34 months; 3 of 10 patients treated surgically showed no improvement but the other 7 recovered, while 4 of 5 patients not operated on also recovered. The removal of a definite disk protrusion seemed to make no difference to the rate or degree of recovery.

The view is expressed that paralysing sciatica is identical in aetiology with the ordinary type of sciatica but is something more than merely an extension of it. It is further suggested that intraradicular haemorrhage may be responsible for the motor manifestations. It is concluded that conservative therapy should be employed in the first instance, but should the condition fail to clear up, surgical exploration may be worth while.

L. A. Liversedge

1400. **Paralysing Sciatica.** (La sciatique paralysante. (Étude de 16 observations))

P. RAVAULT, G. VIGNON, and P. DESLOUS. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **21**, 217–224, March, 1954. 18 refs.

The authors report 16 cases of " paralysing sciatica ", that is, sciatica accompanied by paralysis of the foot, which they believe to be a special clinical form of the disorder. All the cases were encountered in the space of 6 years and affected 10 men and 6 women, most of whom were aged between 38 and 56. In 11 cases the onset of the paralytic episode had been preceded by either lumbago or sciatica. The main clinical features were as follows. (1) Pain of relatively moderate severity was experienced usually in the distribution of the 5th lumbar nerve root, but only in half the cases was there any objective sensory loss. (2) The paralysis in some cases developed within a few hours, in others several days, after the first attack of pain, but might occur at intervals ranging from a few days to 4 months; in one case the paralysis preceded the pain by 6 weeks, and in 6 others appeared simultaneously. In 12 cases the motor disorder was confined to the territory of the lateral popliteal nerve and resulted in weakness of dorsiflexion of the foot and toes, the extensor hallucis muscle being most constantly affected. In 4 cases the medial division of the nerve was also affected. Muscle atrophy was noted in 7 cases, mainly in the anterior tibial region, but seemed to bear surprisingly little relation to the duration of the paralysis. (3) Vasomotor disorder, with oedema and cyanosis, also occurred; this is attributed to affection of the sympathetic fibres in the anterior nerve root.

1401. **Experiences with the Use of 10 per cent. Aqueous Phenol for Chemical Sympathectomy. Preliminary Report**

E. MILES and J. S. ROTHMAN. *American Journal of Surgery* [*Amer. J. Surg.*] **87**, 830–838, June, 1954. 31 refs.

The authors report from Brooklyn, New York, their experience of chemical lumbar sympathectomy in a general surgical service. This treatment was given only to patients with peripheral vascular disease who were considered unfit for open operation and for whom little could be done other than sympathetic interruption. A total of 11 patients, aged from 65 to 75 years, were treated; most were bedridden or confined to the near neighbourhood of their homes. Pain at rest or necrosis due to arteriosclerotic arterial block was present in all but 2. These 2 patients had intractable amputation-stump neuralgia and chronic venous insufficiency respectively; in both cases the history of peripheral vascular disease extended over some 10 years, and both patients also suffered from serious complicating diseases. Procaine nerve block produced negligible increases in skin temperature.

The solution used for chemical sympathectomy was 10 to 15 ml. of 10% phenol; this was injected through a 5-inch 20- or 21-gauge needle, the point of which was manipulated to lie in front of the body of the 2nd lumbar vertebra. Serious pain followed injection in 2 patients: the remainder had no more than slight backache. There were no other complications. Patients were followed up for 6 to 12 months; 8 of the 11 were considered to be improved as to walking ability, relief of pain, and healing of ulceration, and in the patient with venous insufficiency the swelling was much reduced. *C. J. Longland*

Psychiatry

1402. **Clinical Reactions of Schizophrenics to Sodium Amytal, Pervitin Hydrochloride, Mescaline Sulfate, and D-Lysergic Acid Diethylamide (LSD_{25})**
H. H. PENNES. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **119**, 95–112, Feb., 1954. 20 refs.

The effect of three, in some instances four, chemically and pharmacologically dissimilar drugs on each of 55 schizophrenic patients (20 with psychoneurotic schizophrenia, 25 with classic schizophrenia showing little or no deterioration, and 10 with classic schizophrenia but showing severe deterioration) is described in this paper from the New York State Psychiatric Institute. Intravenous injections of amylobarbitone sodium, 0·25 to 0·5 g., "pervitin" (D-deoxyephedrine hydrochloride), 20 or 40 mg., and mescaline sulphate, 0·4 to 0·6 g., were given independently in that order to each of the 55 patients, 25 later receiving in addition D-lysergic acid diethylamide tartrate, 0·01 to 0·12 mg. by mouth.

Although the series was small the results are expressed in percentages [which in some instances do not appear to be exact]. A reduction in symptoms was observed in 65·4% of the patients after administration of amylobarbitone and in 37% after pervitin; there was no reduction in symptoms after administration of mescaline or lysergic acid. The effects lasted 1 to 3 hours with amylobarbitone and 6 hours or more with pervitin. An increase in symptoms was noted in all the patients after mescaline therapy, in 64% after lysergic acid, in 20·4% after pervitin, and in 10·9% after amylobarbitone. But a decrease followed by an increase in symptoms (diphasic response) occurred in 42·6% of patients given pervitin, in 24% given lysergic acid, and in 23·7% given amylobarbitone; no such diphasic responses were obtained with mescaline.

It was found that (1) the same drug induced different reactions in different patients; (2) different drugs sometimes produced the same type of reaction in a given patient; (3) the same drug often had the opposite effect on the same symptom in different patients; and (4) the same patient (in 28 to 31% of cases) showed an increase in symptoms despite chemical and pharmacological differences between the drugs. In many cases the patient's psychological or secondary reactions "seemed to form an important part of the reaction", sometimes continuing after the "direct" or primary effect of the drug should have ceased. *G. de M. Rudolf*

1403. **Indifference to Pain in Low-grade Mental Defectives**
T. A. COUSTON. *British Medical Journal* [*Brit. med. J.*] **1**, 1128–1129, May 15, 1954. 2 refs.

Commenting that the symptom of pain is an important factor in diagnosis, the author then describes 7 cases occurring in mental defective patients at Baldovan Institution near Dundee over a period of 6 months in which there was absence of pain where pain would normally have been expected. The patients were found to be suffering respectively from a fracture of the neck of the femur, a perforated duodenal ulcer, tuberculous enteritis, acute inflammation of a Meckel's diverticulum, a severe head injury sustained in a fall during an attack of grand mal, gross swelling of the left testicle due to torsion, and severe herpes zoster.

The lack of complaint of pain in these cases is compared with that observed in the rare condition known as congenital universal indifference to pain (in which mental defect is absent), and also with the condition after division of the fronto-thalamic projection fibres in partial frontal leucotomy (leucotopectomy). It appears that the fronto-thalamic projection fibres involved in the interpretation of pain and the imposition of pain on consciousness derive from Brodmann's cortical areas 9, 10, and 12, and pass into the dorsomedial nucleus of the thalamus. Thus it is tentatively suggested that the indifference to pain found in low-grade mental defectives suffering from acute surgical or medical conditions may result from defective development either in these frontal cortical areas or in the fronto-thalamic projection fibres.
Adrian V. Adams

1404. **Ulcerative Colitis with Report of a Case**
F. FRANKEL. *British Medical Journal* [*Brit. med. J.*] **1**, 1403–1406, June 19, 1954. 25 refs.

After a review of the literature on the psychosomatic aspects of ulcerative colitis, the author describes a case in which the patient was given psychotherapy and observed over a period of 5 years.

The patient, a woman of 35, had the initial attack of colitis 11 years before she was admitted to the General Hospital, Johannesburg, with the complaint of persistent diarrhoea with blood and mucus in the stool. The findings on physical examination were consistent with a diagnosis of ulcerative colitis. As no improvement followed medication, psychotherapy was started: this consisted in an interview lasting one hour two to three times a week for 10 weeks. Apparently symptoms had first been noted when the patient was 24, after she had refused a proposal of marriage; the reason for this refusal, which was unconscious at the time, was anxiety about leaving her mother. Another attack of colitis coincided with her present husband's proposal; between the proposal and the marriage, symptoms were severe, and the illness continued after marriage.

The psychotherapeutic approach was one of sympathetic understanding and support, the aim being to foster emotional dependence on the therapeutic situation and then to wean the patient from this dependence. The central theme at most of the interviews was the patient's hostile–dependent relationship to her mother; eventually the patient was able to express resentment quite freely. After 4 weeks the colitis subsided, and did not return for 2 years. Mention of a plaque to be erected

to the memory of her mother, who had died, aroused feelings of intense guilt, and next day there was a relapse. After 5 weeks' psychotherapy the colitis again came under control. The patient has remained well for 16 months.

Desmond O'Neill

1405. **Psychotic Response to Attempted Psychotherapy in a Patient with Hyperthyroidism**

J. B. DUGAN. *Psychosomatic Medicine* [*Psychosom. Med.*] **16**, 252–258, May–June, 1954. 1 ref.

A man of 30 with thyrotoxicosis was given psychotherapy consisting in three 1-hour interviews a week. At the first interview the patient himself asked for further sessions, saying that he wanted to talk to a psychiatrist about himself. During the first six sessions the story of his background emerged without much emotional colouring, and his physical condition improved. At the seventh session he was uneasy, and at the eighth he disclosed that his wife was under treatment for syphilis, this admission being accompanied by much feeling. The next day the patient's basal metabolic rate rose, and from this time onward his mental state deteriorated, and over the next week he became psychotic, with disorientation and delusions. It was decided that the thyrotoxicosis was now severe enough to warrant operation, and subtotal thyroidectomy was performed. At the time of the report, 8 months after admission to hospital, the patient was still in a closed ward and still had delusional beliefs.

The author believes that if he had been more aware of the tremendous strength of the patient's " instinctual " forces and the nature of the defences against them, he would have been better able to carry out the treatment. It would appear that touching upon highly-charged conflict themes may precipitate a breakdown, and that therapy should have been kept at a more superficial level until the patient's physical state had improved, or perhaps better omitted altogether until after operation.

[Now that psychiatric methods are being so widely employed in the treatment of these disorders it is important that case records, such as this one, which indicates the possible risks of dealing with emotional forces, should be published in full. The author is to be congratulated on his honesty.] *Desmond O'Neill*

1406. **The Therapeutic Value of Lysergic Acid Diethylamide in Mental Illness**

R. A. SANDISON, A. M. SPENCER, and J. D. A. WHITELAW, *Journal of Mental Science* [*J. ment. Sci.*] **100**, 491–507. April, 1954. 14 refs.

At the Powick Mental Hospital, near Worcester, the authors have used D-lysergic acid diethylamide (LSD25) as a psychotherapeutic aid in treating 36 cases of severe neuroses of poor prognosis or of long duration or resistant to other therapies. The number of treatments —ultimately given weekly—has varied from 2 to 58 for those patients who were improved; duration of illness did not appear to affect the number required, nor did it seem to affect the prognosis with this form of treatment. Apart from what are described as " toxic " effects—that is, those common to most patients—the paper stresses experiences which are regarded as manifestations of each individual patient's unconscious, and which express themselves as hallucinatory experiences, identification and projection phenomena, the reliving of repressed personal memories, and the appearance of impersonal unconscious images (" archetypes "). Depersonalization and " detachment of the conscious self " are also described.

All these experiences are used as adjuncts to psychotherapy of varying depth. Of 23 patients who have completed treatment, 14 are recovered, one is greatly improved, and 6 moderately improved; no improvement was noted in the other 2. The paper includes some comments on a comparison of LSD25 with other psychologically disturbing drugs, a speculative note on the theory of its action, and comments on technique and nursing rules. Case material is quoted. *A. C. Tait*

1407. **Psychological Aspects of the LSD Treatment of the Neuroses**

R. A. SANDISON. *Journal of Mental Science* [*J. ment. Sci.*] **100**, 508–515, April, 1954. 2 refs.

The author surveys the psychiatric material obtained under the influence of D-lysergic acid diethylamide (LSD25) from 36 psychoneurotic patients described in a previous paper [see Abstract 1406]. This upsurge of unconscious material closely resembled dream and fantasy products of patients undergoing deep analysis. Two cases are cited at length in which interpretation of this material was made on Jungian lines, although the author does not exclude other ways of treating unconscious manifestations produced in this way. He believes treatment may not be of any value if the ensuing experiences cannot be understood by the patients. Some comments on the complicated nature of the transference situation are offered. *A. C. Tait*

1408. **Preliminary Observations on the Psychiatric Uses of Chlorpromazine (Largactil)**

D. ANTON-STEPHENS. *Journal of Mental Science* [*J. ment. Sci.*] **100**, 543–557, April, 1954. 2 refs.

The author has used chlorpromazine hydrochloride (" largactil ") in the treatment of 50 cases of schizophrenia, manic-depressive illness, and neurotic syndromes occurring in patients at the Warley Hospital, Brentwood, Essex. The drug was given by intramuscular administration in doses designed to reach a daily total of 200 mg. by the 4th or 5th day, this level being continued for 1 to 7 days, maintenance thereafter being by oral medication. Localized irritation from infection was frequent. Records of 18 cases are cited.

Lessening of disturbed behaviour, decrease in distress, somnolence, and psychic indifference were noted in a number of patients, but usually with relapse on withdrawal of the drug. Side-effects included postural hypotensive attacks, dryness of the mouth, tachycardia, pallor, increase in dreaming, hypotonia, febrile response, and occasionally some fall in the leucocyte count.

The pharmacology of the drug is discussed and the management of patients commented on. [No attempt is made, however, to evaluate the results statistically, nor to list and describe the series as a whole.] *A. C. Tait*

Dermatology

1409. **Isoniazid (Isonicotinic Acid Hydrazide) in Skin Tuberculosis. Preliminary Report of Sixteen Cases**
F. LATAPI, E. ESCALONA, O. RODRÍGUEZ, and S. C. ESTRADA. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **69**, 678–682, June, 1954. 3 figs., 9 refs.

At the General Hospital and the Centro Dermatológico Pascua, Mexico City, isoniazid in a daily dosage of 3 to 8 mg. per kg. body weight was given to 16 patients suffering from tuberculosis cutis, 4 of whom had lupus vulgaris, 4 tuberculosis cutis verrucosa, 4 tuberculosis colliquativa, 2 papulonecrotic tuberculid, one tuberculosis indurativa, and one tuberculosis fungosa. All the patients improved, one with lupus vulgaris, one with tuberculosis colliquativa, and 3 with tuberculosis cutis verrucosa being clinically cured. The drug was more rapidly effective in lupus vulgaris and tuberculosis cutis verrucosa than in the other conditions. No adverse side-effects were seen. *E. Lipman Cohen*

1410. **Adult Premenstrual Acne. An Entity Suggesting Corpus Luteum Dysfunction**
B. A. NEWMAN and F. F. FELDMAN. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **69**, 356–363, March, 1954. 16 refs.

A specific type of acne occurring in women between the age of 20 and the menopause, termed " adult premenstrual acne ", is described in this paper from the Cedars of Lebanon and County General Hospitals, Los Angeles. It is characterized by painless deep papules, without comedo, which sometimes become cystic, occurring on the chin, the sides of the face, and between the eyebrows. The papules appear during the 10 days preceding the onset of menstruation. Spontaneous remission occurs during pregnancy. An injection of 10 mg. of progesterone (10 mg. in 1 ml. of sesame oil) 10 days before the onset of menstruation and another of 5 mg. 5 days before the onset were effective in preventing or controlling the eruption. The authors suggest that corpus luteal deficiency is the causative factor in this type of acne. *Kate Maunsell*

1411. **Multicentric Reticulohistiocytosis of the Skin and Synovia. Reticulohistiocytoma or Ganglioneuroma**
R. W. GOLTZ and C. W. LAYMON. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **69**, 717–731, June, 1954. 5 figs., 19 refs.

The literature on a rare disease entity which has been variously termed generalized giant-cell histiocytosis, reticulohistiocytoma, reticulo-endothelial granuloma, and reticulohistiocytic granuloma, and which may be the same as cutaneous ganglioneuroma, is discussed. Two additional cases are described by the present authors, who propose the term " multicentric reticulohistiocytosis of the skin and synovia ". Altogether 8 certain and 9 doubtful cases have been reported, all in adults. The disease is characterized by large numbers of small nodules and papules in the skin, the former usually being red and the latter skin-coloured. Lesions on the wrists may resemble ganglia. At the same time there is arthritis affecting various joints, usually severely. In some cases abnormality of the thyroid gland is found.

The histological features are constant. In the corium masses of polymorphic cells lie freely in the connective tissue, most of them being histiocytes with large, irregular, pale nuclei. Scattered among these are giant cells with one to 20 nuclei having large, deeply-staining nucleoli and definite nuclear membranes. There are a few lymphocytes and, in some sections, many plasma cells. The capillaries are widely dilated. The collagen fibres are unaffected, but the reticulum fibres are increased in the involved areas. In one of the authors' cases, biopsy of the synovial membrane of a knee-joint showed a layer of histiocytes at the free edges of the membrane adjacent to the joint cavity. Among them were many multinucleated giant cells. Small iron granules were seen to be associated with these cells.
E. Lipman Cohen

1412. **The Cutaneous Manifestation of Pellagra in Chronic Alcoholics.** (Les manifestations cutanées de la pellagre chez les alcooliques)
Y. BUREAU and H. BARRIÈRE. *Presse thermale et climatique* [*Presse therm. clim.*] **91**, 51–55, March–April, 1954. 2 figs.

In the western region of France around Nantes, where a workman may consume 3 or 4 litres of wine a day, pellagra is not uncommon. The cutaneous manifestations usually appear in agricultural workers or fishermen in the spring or early summer, following sudden exposure to intense sunlight. The patients are usually chronic alcoholics and are very often nutritionally deficient, drinking more than they eat. The eruption appears on the exposed parts of the body and consists of erythema, with vesicles or bullae; rarely, the buccal mucosa is affected. In most cases evidence of liver disease is found, and there is usually anorexia, but diarrhoea is rare. Signs of neurological complications, including tremor, delirium tremens, and polyneuritis are present in some cases. The differential diagnosis is discussed. Daily treatment by intramuscular injections of nicotinamide for 2 or 3 weeks, a diet rich in protein, and complete abstinence from alcohol is recommended.
S. T. Anning

1413. **Hexylcaine in Management of Pruritic Dermatoses. Clinical Evaluation of New Local Anesthetic**
I. I. LUBOWE. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **69**, 482–485, April, 1954. 7 refs.

Paediatrics

NEONATAL DISORDERS AND PREMATURITY

1414. **Retrolental Fibroplasia and Oxygen Therapy**
J. T. LANMAN, L. P. GUY, and J. DANCIS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 223–226, May 15, 1954. 17 refs.

An investigation was carried out at Bellevue Hospital, New York, to test the validity of reports that have recently appeared suggesting a relationship between the occurrence of retrolental fibroplasia and intensive oxygen therapy in premature infants. Of the 86 premature infants studied, 21 died before the age of 3 months (that is, before the end of the study); another baby was lost sight of and was excluded from the investigation. The infants were divided impartially into two groups, one receiving 69% of oxygen (standard deviation 6·5%) given continuously for at least 2 weeks or until the infant's weight reached 1,500 g., the other 38% oxygen (standard deviation 7·7%) given only when cyanosis was present. Birth weights ranged from 1,000 to 1,850 g. Two degrees of retrolental fibroplasia were recorded: the early vascular stage, considered to be present whenever vascular dilatation more than twice normal, vascular tortuosity, or haemorrhage into the vitreous or retina was noted after the 10th day of life; and severe, irreversible, cicatricial retrolental fibroplasia.

Of the 64 babies alive at the 3rd month 36 had had high-oxygen therapy and 28 low-oxygen therapy. Of the 36 in the former group, 8 (22%) developed cicatricial retrolental fibroplasia and 22 (61%) passed through the vascular stage; of the 28 in the latter group, none showed cicatricial changes and only 2 (7%) passed through the vascular stage.

There was a mortality of 20% (9 out of 45) among infants receiving high-oxygen therapy, and one of 30% (12 out of 40) among those receiving low-oxygen therapy. This difference is not considered to be significant.

The authors discuss the possible means by which oxygen therapy can cause these toxic effects, and note from their own records that no increase in mortality has occurred since lower concentrations of oxygen have been used as a routine. *H. G. Farquhar*

1415. **Foetal and Neonatal Hepatitis and its Sequelae**
J. H. DIBLE, W. E. HUNT, V. W. PUGH, L. STEINGOLD, and J. H. F. WOOD. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **67**, 195–206, 1954. 11 figs., 9 refs.

A severe type of liver disease occurring in the newborn, which is considered to have been of intra-uterine origin, is described.

Of 5 infants, including 2 siblings, in the acute phase of the disease, 4 died within 2 days of birth. Post-mortem examination showed great loss of parenchymal cells in the liver and their replacement by vascular granulation tissue, resulting in widespread diffuse and almost pericellular fibrosis. Surviving liver cells often appeared as multinucleate masses of varying size, and contained much iron pigment. Islets of regenerating liver cells were also present. Haematopoiesis, which was sometimes marked, was seen.

Histologically the lesions were essentially those of a hepatitis, and from their maturity and the short period of survival, must have developed *in utero*. The histological picture differed, however, from that seen in hepatitis in the presence of the large multinucleated liver cells, the heavy infiltration with stainable iron, and the active haematopoiesis, which was greatly in excess of normal and on a scale similar to that seen in haemolytic disease. No serological evidence of haemolytic disease, syphilis, or congenital obliteration of the bile ducts was found, and it is therefore concluded that these cases were examples of prenatal hepatitis.

To illustrate the postnatal sequelae the authors describe 3 further cases in 2 of which the infants (siblings) were jaundiced and succumbed 3 and 7 weeks after birth. In the liver of the infant who died at the age of 3 weeks well-developed monolobular portal cirrhosis and marked bile-duct proliferation were observed. The liver cells were fatty; there was no haematopoiesis, but a moderate siderosis was present and also gross retention of bile. In the sibling surviving for 7 weeks the picture was similar, except that there was more fibrous tissue and more bile-duct production in the portal tracts. In the third case the histological findings were those of a widespread monolobular cirrhosis, the picture being one of late hepatitis (" subacute yellow atrophy ") in the stage of progression to nodular hyperplasia.

The authors consider these are reasons for believing that foetal and neonatal hepatitis may be the cause of some of the obscure and perplexing types of juvenile cirrhosis. *R. B. Lucas*

CLINICAL PAEDIATRICS

1416. **Sleep in Children of School Age**
G. P. MCLAUCHLAN. *Medical Officer* [*Med. Offr*] **91**, 261–263, June 4, 1954. 6 figs., 3 refs.

An account is given of a study of the sleeping habits of 250 children aged 10½ to 11½ years attending primary schools in Guildford, Surrey. Bed-time varied between 6.30 and 10 p.m., that for the larger number being 8 p.m., and waking time for the majority was between 7 and 8 a.m. There was a large variation in hours of sleep (from 7½ to 12½ hours), with 11 hours recorded for 87 of the group. Reference is made to changes in the electroencephalographic pattern during sleep, and it is concluded that the child difficult to waken in the morning has not completed his sleep cycle. Of the 250 children studied, only 13 were difficult to waken.

On the assumption that there is a definite correlation between insufficient sleep and a poor appetite for breakfast, the sleeping habits of 49 children difficult to waken or having a poor appetite for breakfast (Group B) were contrasted with those of the remaining 201 children (Group A). It was found that only 57% of Group B fell asleep within 30 minutes as compared with 80% in Group A (reading in bed was excluded as an important factor). Neither sharing a room nor sharing a bed was considered to contribute to lack of sleep.

The author concludes that it is not possible to generalize as to how much sleep children need or to be dogmatic in fixing their bed-time. *F. T. H. Wood*

1417. **Idiopathic Hypercalcaemia of Infants. Low-calcium Treatment**

A. W. FERGUSON and G. K. MCGOWAN. *Lancet* [*Lancet*] **1**, 1272–1274, June 19, 1954. 2 figs., 4 refs.

The cause of idiopathic hypercalcaemia in infants is unknown, but since many of the symptoms may be due to the high blood calcium level it appeared reasonable to the authors to try the effect of a low-calcium diet. Milk has a high calcium content, and they therefore describe two methods of producing types of milk containing less than 5 mEq. of calcium per litre. In the first fresh milk was run through a column of cation-exchange resin so that calcium was exchanged for potassium, sodium, and magnesium. In the second a commercial " low-ash casein " containing only traces of calcium was used, to which cream, lactose, and various salts were added so that the final composition was similar to that of human milk, except for the low calcium content.

At the Children's Hospital, Bristol, 4 infants were treated with these prepared milks, receiving in addition iron, ascorbic acid, " marmite ", and carbohydrate. All the children responded promptly, and rapidly gained weight. The authors point out that these results must be interpreted with caution because spontaneous recovery is usual. Moreover, as the artificial milks lack various natural ingredients they should gradually be replaced by ordinary cow's milk after about one month.

A. Paton

1418. **Inguinal Hernias in Infants and Children. A Critical Study of 250 Patients Treated by Surgery**

W. D. DUNAVANT and H. WILSON. *Journal of Pediatrics* [*J. Pediat.*] **44**, 558–562, May, 1954. 1 fig., 8 refs.

The authors review 250 cases of inguinal hernia occurring among children up to 12 years of age operated upon during the past 5 years at the John Gaston Hospital, Memphis (University of Tennessee). The hernia occurred on the right side in 70%, the left side in 26%, and was bilateral in 4%; 233 (93%) of the patients were boys. Cryptorchidism was present in 5 cases and an associated hydrocele in 9 cases. Irreducible herniae were present in 89 cases, in 85% of which the patient was under 2 years of age. The incidence was highest under 6 months of age, when more than three-fourths were irreducible. Spontaneous reduction before operation took place in 26 cases. In no case was an intestinal resection necessary. One postoperative death occurred in the series.

Because of the high incidence of incarceration in infancy the authors advocate operative treatment for inguinal hernia at whatever age the diagnosis is made; early age is not regarded as a contraindication. They consider that high ligation with excision of the sac is the treatment of choice; only occasionally is a repair of the muscle layers necessary. Recurrence occurred in 2 cases in the series, these being the only cases in which ligation of the sac (with silk) was not accompanied by its excision. In the presence of strangulation the importance of investigating fluid and electrolyte imbalance is stressed; an attempt to correct this should precede any operative treatment.

[Unfortunately no clear distinction is drawn between the terms " irreducible ", " incarcerated ", and " strangulated " hernia. This confusion also exists in earlier papers to which reference is made.]

M. A. Birnstingl

1419. **Intestinal Obstruction due to Ascariasis. Report of Thirty-one Cases**

M. Q. JENKINS and M. W. BEACH. *Pediatrics* [*Pediatrics*] **13**, 419–425, May, 1954. 1 fig., 16 refs.

Ascariasis is due to ingestion of the ova of *Ascaris lumbricoides* from soil polluted by human sources. The larvae are released from the ova in the small intestine of the host, enter the lymphatics, and pass through the heart to the pulmonary capillaries, from which they emerge into the alveoli. They ascend the trachea, are swallowed, and mature in the small intestine where they live on chyme. The females mature and lay eggs in about 70 days. The adult ascaris is 15 to 40 cm. long and aggregations of ascarides cause intestinal obstruction, intussusception, volvulus, perforation, biliary and pancreatic obstruction, and abscesses in the liver and lungs.

From the Medical College of South Carolina, Charleston, the authors report 31 cases of partial small bowel obstruction due to ascariasis in patients aged 18 months to 9 years. The diagnosis was based on a history of excretion of round worms at some time or on the finding of ova on microscopical examination of the stool. The usual symptoms were vomiting, diarrhoea, abdominal distension, with a palpable doughy mass. Adult ascarides were vomited by 5 patients. Radiographs revealed gas fluid levels and occasionally worms. Symptoms were often precipitated by a vermifuge or by intercurrent infection.

Except in 3 cases in which appendicitis was suspected and 2 in which obstructive symptoms persisted, treatment was conservative. For 24 hours continuous gastric suction was carried out and fluids were administered intravenously. This was followed by administration of hexylresorcinol to 18 patients, and " hetrazan " (1-diethylcarbamyl-4-methyl piperazine hydrochloride) to 10. Small doses of hexylresorcinol were given at first, repeated on alternate days if necessary. After distension was relieved and a normal stool had been passed, the full dose of hexylresorcinol (0·1 g. per year of age) was given, followed in 4 hours by a dose of magnesium sulphate. The dosage of hetrazan was 6 mg. per kg. body weight

three times a day. It is claimed that hetrazan in this dosage is not toxic, and is easy to administer; moreover the ascarides passed in the faeces are alive, thus absorption of toxic products from dead ascarides is avoided. No starvation or purgative is necessary.

In the authors' view conservative treatment is usually effective and safe, but operation may be necessary for appendicitis or persistent obstruction. In one case a portion of the ileum was distended and discoloured; 125 ascarides were removed through an enterotomy and the colour of the bowel became normal. A second operation was, however, required 3 weeks later because of adhesions. One patient in the series died from dehydration and another from inhalation of ascarides during vomiting. *Charles P. Nicholas*

1420. **A Study of Cross-infection with Type Strains of *Bacterium coli* in Gastro-enteritis Wards**
T. ANDERSON, H. CROCKATT, and C. A. C. ROSS. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **68**, 1–15, 1954. 5 refs.

At the Ruchill and Knightswood Hospitals, Glasgow, shortage of cubicle accommodation has necessitated the admission of infants with gastroenteritis to open wards used exclusively for this purpose, so that babies with a mild, non-specific infection are nursed side by side with infants from whose faeces specific types of *Bacterium coli* have subsequently been isolated. Under these conditions the authors have studied the incidence of cross-infection due to *Bact. coli* O111, O55, and O26 in three such wards. In addition, as the three wards differed considerably in nursing routine and efficiency, it was hoped that a comparison of the end-results might afford information as to the mode of spread of these organisms. During the period of investigation a total of 425 infants were admitted.

Stringent criteria were adopted for the isolation of the type strains of infective *Bact. coli*. The commonest of the three pathogenic strains and the one causing the most serious illness was Type O111. This was present on admission in 94 of the 425 infants, causing severe symptoms in 35 and death from the initial illness in 8. Type-specific *Bact. coli* were present in faecal specimens taken on admission in altogether 135 cases (31·8%); 9 of these patients died from the initial illness. In 290 cases none of these types of *Bact. coli* were present in the stools when the patient was admitted; of these cases 7 proved fatal.

Cross-infection was considered to have taken place: (1) if a baby from whom none of the *Bact. coli* types was isolated on admission subsequently acquired one of them; (2) if a baby from whom a specific type was isolated on admission subsequently acquired a different specific type; or (3) if a baby, after a minimum clearance interval of 2 weeks, was again found to excrete the same type as that originally isolated.

There were altogether 127 cross-infection incidents involving 114 (26·8%) of the infants admitted. The cross-infection caused severe symptoms in 16 of the babies and 5 of them died. Type O111 was again the most dangerous organism and caused all the deaths. There was no difference in the incidence of cross-infection between babies with initially negative and those with initially positive stools. The cross-infection rates were highest (34%) in the ward which was considered to be the most efficiently run, but against this should be placed the fact that babies in that ward were kept in hospital for longer periods. No correlation was found between susceptibility to cross-infection and age.

It is suggested that every effort should be made to prevent the admission to hospital of babies suffering from mild attacks of diarrhoea and vomiting. The authors doubt whether cubicle isolation of each child would solve the problem of cross-infection, and do not consider either that treatment with the newer antibiotics would help or that admission of such babies to wards containing older children or adults would be practicable.

[This article should be studied in full by those interested; it is a careful analysis of the problem on the basis of statistical evidence]. *John Lorber*

1421. **Duodenal Ulcer in Children with Hemorrhage as the Presenting Symptom. Report of Three Cases**
E. L. MARCUS. *Journal of Pediatrics* [*J. Pediat.*] **45**, 75–79, July, 1954. 5 refs.

1422. **The Use of a Cation Exchange Resin in the Management of Anuria in Childhood**
W. B. MACDONALD and M. J. ROBINSON. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **3**, 123–130, May, 1954. 5 figs., 14 refs.

The authors describe the treatment at the Royal Children's Hospital, Melbourne, of the hyperpotassaemia of anuria in 6 children, 5 of whom suffered from acute glomerulonephritis and one from polyarteritis nodosa. In 5 of these cases the potassium intoxication was treated by administration of a cation-exchange resin in either the ammonium or the sodium cycle. Of these 5 patients, 2 subsequently died. The treatment in the remaining case was that generally used in the modern management of anuria.

Of the 5 children treated with cation-exchange resin, one had a serum potassium value of 8·3 mEq. per litre by the 11th day of anuria; 45 g. of resin was then given at 8-hourly intervals, while measures were taken to avoid acidosis, hyponatraemia, and hypocalcaemia. The serum potassium level fell in 2 days to 6·4 mEq. per litre; the sodium level also fell. Urine flow was re-established later. In another patient 3 days' treatment reduced the potassium level from 9·4 to 8·8 mEq. per litre. In a further case, although there was some flow of urine, the potassium level nevertheless increased. After administration of resin had reduced the level to 3·5 mEq. signs of potassium depletion became apparent. Two other cases of anuria were treated with similar results. In 3 cases in which the faeces were analysed they were shown to contain a large amount of potassium during the period of treatment.

The authors, who sound a warning against over-treatment, conclude that the resin in the sodium cycle is probably more satisfactory than the ammonium variety in the treatment of these cases. *G. Loewi*

Public Health

1423. **Enforced Legal Isolation of Tuberculous Patients**
E. KUPKA and M. R. KING. *Public Health Reports* [*Publ. Hlth Rep.* (*Wash.*)] **69**, 351–359, April, 1954. 10 refs.

A number of States in the U.S.A. have laws for the compulsory isolation of tuberculous patients, but the full authority of the law is rarely applied. Los Angeles County has tried the experiment (known as the California Experiment) of enforcing its authority.

In the compulsory isolation of recalcitrant tuberculous patients a number of problems had to be faced; for example, few prisons had adequate hospital facilities, and few sanatoria could prevent patients from escaping. Many patients upon whom court orders have to be served have complicating circumstances—for example, chronic alcoholism. Through the cooperation of the State's Department of Corrections a suitable institution was usually found, and although " a local obstacle was presented by those country prosecuting attorneys and judges who were reluctant to send sick tuberculous patients to a prison " the scheme has achieved results. Of these, the reduction in the number of patients who refuse to be isolated—brought about by the threat of execution of the order—is possibly the most important.

The legal position is discussed and a brief summary of the various laws given. *Scott Thomson*

VITAL STATISTICS

1424. **The Mortality of Doctors in Relation to Their Smoking Habits. A Preliminary Report**
R. DOLL and A. BRADFORD HILL. *British Medical Journal* [*Brit. med. J.*] **1**, 1451–1455, June 26, 1954. 1 fig., 13 refs.

Previous studies of the smoking habits of patients with cancer of the lung and of those without this disease have shown that among the former group there was a greater proportion of heavy smokers and a smaller proportion of non-smokers than in the latter group. The present authors now add further evidence of a relationship between smoking habits and subsequent death from lung cancer in this preliminary report of a prospective study. At the end of 1951 members of the medical profession in the United Kingdom were invited to complete a questionary in which he was asked to classify his smoking habits as (*a*) " smoking at present ", or (*b*) " smoked in the past but now stopped ", or (*c*) " never smoked " (" smoking " being defined as not less than one cigarette a day, or its equivalent in pipe tobacco, for as long as one year). The smokers were also asked to state the age at which they started smoking and the amount and method of smoking, and ex-smokers the age at which they stopped smoking. The questions were intentionally simple and limited in number in order to encourage response, but further voluntary information likely to be of interest was invited.

According to their replies the doctors were classified by age, amount smoked, method of smoking, and whether present or past smokers, these forming the group " exposed to risk " of the study, the purpose of which was to compare the mortality of doctors in the various subgroups of the classification during the years ahead. The six Registrars-General of the various parts of the United Kingdom have agreed to give particulars of the cause of every doctor's death registered since 1951, and from this the death rates from cancer of the lung and some other diseases have been calculated for different ages and smoking categories. It is emphasized that this is essentially a preliminary report, being based on the deaths reported only in the first 29 months, and confined to male doctors aged 35 and over, from whom a total of 24,389 relevant replies were received. Of the whole group, 12·7% were classified as non-smokers, in 34·6% the daily average consumption of tobacco was 1 to 14 g. (1 g. equals roughly 1 cigarette, and 1 oz. (28 g.) of pipe tobacco per week was taken to equal 4 g. per day), in 31·4% it was 15 to 24 g., and in 21·3% it was 25 g. or more. Of the smokers 16·7% smoked pipes, 21·2 smoked pipes and cigarettes (cigar smokers were included here), and 62·1% smoked cigarettes only. These distribution figures are not necessarily representative of all doctors, but this fact does not invalidate their use in the present study.

In the first 29 months of the experiment there were 789 deaths of male doctors who were aged 35 years and over and exposed to risk. Of these, the cause of death was classified as follows: cancer of the lung 36, other cancers 92, disease of the respiratory system (other than cancer) 54, coronary thrombosis 235, other cardiovascular diseases 126, and all other diseases 247 (one case of lung cancer, registered as a contributory cause of death, was included twice). These death rates, standardized for age, were correlated with the numbers in the four groups, that is non-smokers, and smokers consuming an average of 1 to 14 g., 15 to 24 g., and over 25 g. of tobacco per day. It was shown that the death rate from cancer of the lung increased consistently and steeply with the amount of tobacco smoked, the respective figures for the four groups being 0·00, 0·48, 0·67, and 1·14 deaths per annum per 1,000 men aged 35 and over. A similar although less steep increase occurred for coronary thrombosis, the figures here being 3·89, 3·91, 4·71, and 5·15 per annum per 1,000. In the other four disease groups considered the differences between the various smoking groups were small or the trends irregular; but it is emphasized that when more data have accumulated further subdivision, particularly of the " other cancers " and the " respiratory " groups, will be of great interest. For these two groups the rates in order of increasing amount of tobacco smoked were

2·32, 1·41, 1·50, and 1·91 per 1,000 per annum for " other cancers ", and 0·86, 0·88, 1·01, and 0·77 for " respiratory disease ". After the application of appropriate tests of significance it is concluded that, taking P as 0·05, the trend of increasing mortality with increasing amount of tobacco smoked is significant for lung cancer and suggestive for coronary thrombosis.

Because of the limited number of deaths available for study, its was not possible to examine with sufficient accuracy the effect of different methods of smoking—a study which is further complicated by the difficulty of isolating " pure " cigarette smokers from " pure " pipe smokers because of changes in smoking habits. But taking the data at their face value the 36 men dying of cancer of the lung appeared to include an excess of cigarette smokers and a deficit of pipe smokers, although the differences were not significant.

The mortality trends for lung cancer in the present enquiry are in conformity with estimations made in earlier retrospective studies, although generally the level of mortality among doctors in each smoking group in the present survey was lower. Evidence is put forward, however, that the mortality reported in this study is almost certainly understated because of " reluctance, or inability, of persons suffering from a fatal illness to reply to the questionary ".

[This is an important contribution to the aetiology not only of lung cancer, but also of other diseases, and with its accompanying tables should be studied in the original to be properly appreciated. With characteristic thoroughness the authors examine several sources of possible bias and give details of the various statistical tests of significance which cannot be included in an abstract.] *E. A. Cheeseman*

EPIDEMIOLOGY AND IMMUNIZATION

1425. **Variations in Age Distribution of Poliomyelitis. Comparative Ratios of Younger and Older Age Groups**
M. SIEGEL and M. GREENBERG. *Journal of Pediatrics* [*J. Pediat.*] **44**, 658–664, June, 1954. 5 figs., 5 refs.

An investigation was undertaken by the New York City Department of Health to provide comparative data which would show the annual trend of newly reported cases of poliomyelitis during recent epidemics in the city, the aim being to evaluate the claims of the beneficial effect of mass administration of gamma globulin. In all, 8,964 confirmed cases notified during the years 1944–52 were analysed. As a reduction in the incidence in the younger age groups had been reported, the cases were divided into two groups according to age of the patients, namely, from 0 to 10 years, and from 10 years upwards, both groups comprising both paralytic and non-paralytic cases. The case fatality rate ranged from 3·3 to 7·3% (average 5·6%) and the mortality per 100,000 of the population from 0·1 in 1947 to 2·2 in 1949. The date of onset was known in 8,851 cases (98·7%).

A study of the seasonal variation for all years and all cases taken together showed that the incidence began to rise in the later part of June and reached a peak in the 34th and 35th weeks of the year, that is, towards the end of August. But a more detailed investigation by age groups revealed a striking difference in the incidence curve for the two groups. Whereas the younger patients, up to the age of 10 years, showed a high percentage distribution of cases early in the poliomyelitis season, a low point in the 35th week, and another rise in late September (40th week), the older patients showed the reverse trend. In view of this difference in incidence between the two age groups the authors give a warning that any conclusions drawn from the observation of a slight decline in the occurrence of poliomyelitis in the younger age group following the use of prophylactic measures should be treated with caution. *E. Hoffa*

1426. **An Outbreak of Trichinosis in Liverpool in 1953**
A. B. SEMPLE, J. B. M. DAVIES, W. E. KERSHAW, and C. A. ST. HILL. *British Medical Journal* [*Brit. med. J.*] **1**, 1002–1006, May 1, 1954. 8 figs., 5 refs.

An outbreak of trichinosis occurring in Liverpool in the autumn of 1953 is described; the epidemiological evidence indicated that the source of the infection was sausages or sausage meat made by a local firm. In 16 of the total of 82 cases the diagnosis was confirmed by demonstration of larvae in a muscle biopsy specimen. Inquiry revealed that in 34 cases the sausage meat was eaten raw and in 33 it was cooked; 2 affected persons denied eating sausages or sausage meat, but there was some evidence that they had bought pork from the same source; the remainder had handled infected sausage or eaten ham handled by employees of the firm supplying the sausage meat. As most (62) of the affected persons were housewives and over half of them had eaten or tasted raw sausage, some 3,000 housewives in the district were questioned, and 16% admitted to the habit of eating or tasting raw sausage.

The cases were recognizable clinically. All the affected persons had swelling of the eyelids and nearly all had severe headache, and some had muscle pain. Eosinophilia, varying from 550 to 12,000 eosinophils per c.mm., was present in all but 4 cases; in these the diagnosis was confirmed at biopsy. *Scott Thomson*

1427. **Measles in the Canadian Arctic, 1952**
A. F. W. PEART and F. P. NAGLER. *Canadian Journal of Public Health* [*Canad. J. publ. Hlth*] **45**, 146–156, April, 1954. 6 figs., 6 refs.

This paper contains an account from the Canadian Department of National Health and Welfare, Ottawa, of an outbreak of measles among Eskimos in settlements along Ungava Bay and the southern coast of Baffin Island. The outbreak occurred in winter when weather conditions were at their worst, but in face of great difficulties gamma globulin was given to several hundred contacts and injections of antibiotics were given to many others.

The attack rate was 99%, with a case mortality rate of 7% at Ungava Bay and of 2% in Baffin Island. In the latter the mobilized medical resources may have played a part in keeping the rate low. The outbreak began

when 2 Eskimos incubating measles returned from an air base in Labrador. Thereafter, because of the conditions of living, it was possible to trace the movements of people from village to village and follow the spread of the disease. *Scott Thomson*

1428. **Colds among Office Workers. An Epidemiological Study**
D. D. REID, R. E. O. WILLIAMS, and A. HIRCH. *Lancet* [*Lancet*] **2**, 1303–1306, Dec. 19, 1953. 2 figs., 4 refs.

An account is given of an investigation carried out on behalf of the Air Hygiene Committee of the Medical Research Council into the incidence of the common cold in a group of 131 office workers in the City of London during the one-year period April, 1949, to March, 1950. A method of obtaining precise information relating the incidence to environmental measures was explored, the workers being questioned weekly as to upper respiratory symptoms in themselves and their contacts.

The following observations were recorded. On the average each person had 2·2 colds in the year, the incidence of "colds" appearing to be highest in young women. Although there was evidence of short-term immunity following a cold, no other differences in range of contact at work, during travelling, or at home appeared to affect the attack rate. The beginning of a sharp epidemic of colds in November, 1949, coincided with a fall in outside temperature and humidity; at the same time there was a rise in the count of *Streptococcus salivarius* in the office air. *E. V. Saunders-Jacobs*

1429. **The Distribution of Carriers of *Streptococcus pyogenes* among 2,413 Healthy Children**
M. C. HOLMES and R. E. O. WILLIAMS. *Journal of Hygiene* [*J. Hyg.* (*Lond.*)] **52**, 165–179, June, 1954. 16 refs.

An investigation was carried out at the Streptococcal Reference Laboratory, Colindale, London, to determine the incidence among healthy children of carriers of *Streptococcus pyogenes* in the nose and throat. For this purpose single throat and nasal swabs were taken from 2,413 healthy children during the 11 weeks from Oct. 3 to Dec. 16, 1949, in three north-west London boroughs. Throughout the analysis standard statistical methods were used. Most of the analyses referred to "standardized" and not actual rates, to allow for the separate assessment of several interrelated factors. The assessment of the social class was not according to the Registrar-General's classification, but was based on the types of schools the children attended and on their housing standards.

A history of rheumatic fever was obtained in only 13 of 1,793 schoolchildren (0·73%). Of the 2,413 children, 100 (4·2%) were nasal carriers and 496 (20·6%) throat carriers of *Streptococcus pyogenes*. The mean nose and throat carrier rates rose between the first and last 4-week periods of the survey, from 1·6 and 15·1% to 7·3 and 23·3% respectively. Very much lower carrier rates were found in young children at home than in those of the same age who were attending schools or day nurseries. Significantly higher carrier rates were found in children in whom the tonsils were present (28% and 3·8% respectively) than in those without tonsils (7·9% and 1·6%). An apparent increased nose and throat carrier rate in children from lower social classes disappeared when the figures were standardized according to whether tonsillectomy had been performed or not. The highest nasal carrier rates occurred in the 3- and 4-year-old children attending day nurseries.

No conclusion could be reached as to whether an increased incidence of streptococcal carriers amongst healthy children represents an increased risk of streptococcal tonsillitis or of rheumatic fever. *John Lorber*

1430. **Staphylococcal Food-poisoning due to Infected Cow's Milk**
F. D. F. STEEDE and H. W. SMITH. *British Medical Journal* [*Brit. med. J.*] **2**, 576–578, Sept. 4, 1954. 8 refs.

1431. **Effectiveness of Polyvalent Influenza A Vaccine during an Influenza A-prime Epidemic**
G. MEIKLEJOHN, C. H. KEMPE, W. G. THALMAN, and E. H. LENNETTE. *American Journal of Hygiene* [*Amer. J. Hyg.*] **59**, 241–248, May, 1954. 2 figs., 4 refs.

From the autumn of 1948 studies were conducted each winter at Fort Ord (a military training depot), California, for the purpose of evaluating influenza virus vaccines. In the winter of 1949–50 an epidemic caused by the influenza A-prime virus occurred, when the incidence of clinical infection was found to be lower among personnel who had been immunized with a monovalent FM-1 (A-prime) virus vaccine than among those who received PR8 (A) vaccine, Lee (B) vaccine, or saline (*Amer. J. Hyg.*, 1952, **55**, 12; *Abstracts of World Medicine*, 1952, **12**, 8). On the basis of this finding the plan of study was modified during the next winter. New arrivals at the camp were divided into three roughly equal groups given respectively: (1) a polyvalent influenza-A vaccine containing PR8, FM-1, and Cuppett (FW-1-50) strains; (2) a monovalent influenza-B vaccine prepared from the Lee strain; and (3) a formalin–saline solution. An outbreak of influenza of A-prime type occurred between January and March, 1951, and the present report is concerned with the incidence of infection in these three groups during that outbreak. The findings were as follows.

Among the 2,596 subjects in Group 1 (immunized against influenza A) 13 cases (0·5%) of clinical infection occurred; among 2,600 in Group 2 (given influenza-B vaccine 54 cases (2·1%) occurred; and among the 2,628 control subjects there were 51 cases (1·9%). The numbers of cases of other respiratory infections occurring during this outbreak were: Group 1, 77 (3%); Group 2, 91 (3·5%); and Group 3, 68 (2·6%).

In view of their earlier experiences the authors do not consider that the PR8-strain vaccine contributed towards the reduction in incidence observed in Group 1, but that this should be attributed to the two A-prime strains. They conclude that a significant reduction in the incidence of influenza during epidemics of the A-prime type can be obtained by immunization with appropriate vaccines prepared from A-prime strains. *Franz Heimann*

Industrial Medicine

1432. **Working Capacity and Rehabilitation of Persons with Hypertension.** (Принципы оценки трудоспособности и трудоустройство при гипертонической болезни)
L. I. FOGEL'SON. *Терапевтический Архив* [*Ter. Arkh.*] **26**, 46–50, March–April, 1954.

In a series of 980 hypertensive persons of various professions the blood pressure was determined periodically before, during, and after daily work.

From the results of this investigation the author concludes as follows. Routine work, involving a moderate degree of physical exertion only and carried out during the morning shift, often led, in mildly hypertensive subjects, to a decrease in blood pressure of about 10 to 30 mm. Hg systolic and 5 to 15 mm. Hg diastolic; but such a decrease was not observed if the work involved nervous tension. In similar circumstances, work during the night shift tended to produce a rise in blood pressure. Nervous and psychological tension tended to aggravate hypertensive disease, as was shown by a comparison of the daily blood pressure readings before and after work. Moderately hypertensive patients were found to be more susceptible to the comparatively slight stress and strain even of routine work. "Negative emotions" experienced during work produced a transient, but considerable, rise in blood pressure. Normal control subjects manifested no changes in blood pressure during a working day. *A. Swan*

1433. **Blood Pressure in Different Professional Groups.** (О кровяном давлении у различных профессиональных групп)
V. A. SHTRITER. *Терапевтический Архив* [*Ter. Arkh.*] **26**, 50–55, March–April, 1954.

The author reports the results of an analysis of blood-pressure readings of 25,937 factory workers (13,439 men and 12,498 women) which were recorded during the decade 1936–46. Only systolic pressures were considered for, as the author puts it, "changes in the diastolic level did not materially differ from those in the systolic pressure". The limits of normal systolic pressure were arbitrarily fixed at 100 to 140 mm. Hg.

Before the war high blood pressures were recorded in only 9% of male workers, while up to 17% were assessed as "hypotensive". During the war years the proportion of sufferers from high blood pressure rose sharply, reached its maximum in 1943, and thereafter declined, but even in 1946 it was 50% higher than in 1936. A rise in the incidence of hypertension was observed as early as 1940, that is during the war with Finland, when there was as yet no widespread malnutrition.

The incidence of hypertension was found to increase rapidly with age; thus, in 1943–4, 88·7% of individuals in the age groups above 50 were found to have hypertension, whereas for the age group 20–29 this figure was only 5·7% (ratio 15·6 to 1). The respective figures for 1946 were 53·1% and 3·1% (ratio 17·2 to 1). Men and women were found to be equally prone to develop high blood pressure. Hard physical labour and work associated with nervous tension were found to favour the development of hypertension.

Some tendency to hypotension was found among lead workers (5,428 cases), and also among those in contact with benzole derivatives. Industrial contact with mercury, aromatic nitro-compounds, and carbon disulphide did not appear to affect the blood pressure. *A. Swan*

INDUSTRIAL TOXICOLOGY

1434. **Toxicology of Mono-, Di-, and Tri-propylene Glycol Methyl Ethers**
V. K. ROWE, D. D. MCCOLLISTER, H. C. SPENCER, F. OYEN, R. L. HOLLINGSWORTH, and V. A. DRILL. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg.*] **9**, 509–525, June, 1954. 1 fig., 10 refs.

An investigation was undertaken at Midland, Michigan, to evaluate the hazards associated with the manufacture, handling, and use of the monomethyl ethers of monopropylene, dipropylene, and tripropylene glycols. These compounds are stable liquids, and because they are miscible with a wide variety of solvents, including water, they are coming to be increasingly used for industrial purposes. Experiments on animals were performed to assess the probable toxicological effects of these liquids, with the following results.

For rats the LD_{50} of single doses by mouth was found to be 6·6 ml. per kg. body weight for monopropylene glycol methyl ether (33 B), 5·4 ml. per kg. for dipropylene glycol methyl ether (50 B), and 5·3 ml. per kg. for tripropylene glycol methyl ether (62 B). When 1 ml. of 33 B per kg. was given daily by mouth on 5 days a week for 35 days no ill effects were observed in these animals.

The undiluted liquids produced only mild transitory irritation in the eyes of rabbits. Although the compounds are absorbed through the skin, it was found that relatively large amounts had to be applied to produce toxic effects. In the case of 33 B, applications of 10 ml. per kg. to the skin of rabbits caused only narcosis, but 15 ml. per kg. killed most of the animals. Even larger applications of 50 B and 62 B were not lethal. When the applications were repeated daily 33 B was well tolerated at a dose of 2 ml. per kg. body weight. In no case was skin irritation observed, and it proved impossible to sensitize human subjects in this way.

When animals were exposed on a single occasion to the vapour of 33 B they showed signs of depression of the central nervous system and some irritation of mucous surfaces. On repeated exposure to this vapour for 7 hours a day on 5 days a week for 6 months it was shown

that guinea-pigs tolerated 3,000 parts per million (p.p.m.), rats 1,500 p.p.m., and monkeys and rabbits 800 p.p.m., without adverse effects. Similar exposures to an atmosphere saturated with 50 B (300 to 400 p.p.m.) produced minimal ill effects in the same species.

It is concluded that these three compounds as used commercially present no hazards to health. Although they have pronounced narcotic properties, they produce only trivial injuries in the respiratory tract and liver. Moreover, any concentration of their vapour likely to be toxic to man would produce enough irritation to act as a satisfactory warning. *W. K. S. Moore*

1435. **Neurological Aspects of Industrial Manganese Poisoning.** (Aspects neurologiques de l'intoxication professionnelle par le manganèse)
J. BOYER and J. RODIER. *Revue neurologique* [*Rev. neurol.* (*Paris*)] **90**, 13–27, 1954. 5 figs.

The authors report, from the Institute of Hygiene, Morocco, 21 cases of chronic manganese poisoning among miners of the ore, with particular reference to early symptoms and neurological signs, 3 cases being described in some detail. Emphasis is placed on the importance of recognizing the early manifestations of poisoning so that workers may be removed from contact with the ore and advantage thus taken of a possible remission in an otherwise inexorably progressive disease. The earliest symptoms are largely subjective, consisting in vague pains, apathy, and later, dysphonia. Difficulty in walking, particularly backwards or down an inclined plane, in sitting down on a chair, and in squatting constitute some of the important early signs, and there is often a fixed expression of euphoria punctuated by spasmodic smiles.

The neurological evidence suggests that chronic manganese poisoning results in disseminated lesions of the central nervous system affecting principally the extrapyramidal tracts, but also the pyramidal system in some cases, and the cortical and subcortical areas. Metabolic and endocrine disorders (such as hypogenitalism) were also found in many of the cases, but whether these are the cause of the nervous involvement or the result of it is still undecided. The role of metabolic disease in the production of nervous disorders is discussed. In discussing the differential diagnosis the authors remark that despite the absence of Kayser–Fleischer rings in the cornea, and the lack of evidence of hepatic disorder, the likeness of chronic manganese intoxication to Kinnier Wilson's hepato-lenticular degeneration is notable.

[The original article should be referred to for its excellent descriptions of the physical signs.]
W. K. S. Moore

1436. **The So-called Benzene Pneumonia.** (Клиника так называемых бензиновых пневмоний)
E. I. BICHUNSKAYA. *Терапевтический Архив* [*Ter. Arkh.*] **26**, 79–84, March–April, 1954. 6 refs.

"Benzene pneumonia" appears to be a form of aspiration pneumonia. Patients usually give a history of having aspirated some of the fluid when attempting to establish a syphon by sucking through a rubber tube, as in emptying a container such as the petrol tank of a car. The author reports 17 such cases, and refers to 17 further cases described by other workers.

The clinical picture of the illness in these cases was characteristic. After an initial period of severe, irritating cough lasting for about 20 or 30 minutes, sometimes with vomiting, there was a silent interval of 2 to 3 hours, after which the patients experienced pain on respiration, usually in the right side of the chest. Later rigor, headache, a burning sensation behind the sternum, and general dyspnoea were complained of. On admission to hospital the patients showed cyanosis, rapid breathing, reduced mobility of the right side of the chest. The temperature ranged from 38° to 39° C. (100·4° to 102·2° F.), and a pleuritic rub was invariably observed. Pneumonia was bilateral in only one case, and occurred in one case on the left side; in the remaining 15 cases it was on the right side only, and usually in the middle lobe. The course was usually benign, and by the end of the first week the temperature had returned to normal. Complete recovery in some cases, however, was delayed.

Of 15 patients who swallowed petrol, but did not aspirate it, none developed pneumonia, nor did any of 22 rats in which the fluid was introduced into the stomach by intubation. The author concludes that, in spite of the fact that petrol when swallowed is excreted by way of the lungs and may produce pulmonary congestion (and in rats bronchitis), its direct aspiration is necessary for pneumonia to develop. *A. Swan*

OCCUPATIONAL DISEASES

1437. **Raynaud's Phenomenon Due to Vibrating Tools. Neurological Observations**
J. MARSHALL, E. W. POOLE, and W. A. REYNARD. *Lancet* [*Lancet*] **1**, 1151–1156, June 5, 1954. 2 figs., 13 refs.

The authors report from the Oxford United Hospitals a clinical survey of 37 men suffering from Raynaud's phenomenon, the diagnosis of which was made on the history alone. The condition was found to be present in 29 out of 31 men using a pneumatic hammer delivering 2,300 blows per minute, and in 8 out of 9 men using a trip hammer [the frequency of which is not stated]. Sensory loss in the affected fingers was estimated (*a*) by the assessment of the sense of light touch, made with graded nylon threads, and of the response to pinprick, using a standard needle variously weighted; and (*b*) from the time of onset of numbness due to ischaemia after application of a sphygmomanometer cuff. In addition 4 men were examined by means of a nerve clamp which rendered a segment of the ulnar nerve in the upper arm ischaemic.

There are two views of the causation of Raynaud's phenomenon, one being that it is due to a local fault in the condition of the digital arteries, the other that overactivity of the vasomotor nerves is the primary cause. From the fact that in the cases examined a permanent sensory deficit was common in association with Raynaud's phenomenon, the present authors conclude that lesions in the peripheral nerves are the probable cause.

Motor weakness was also elicited in the abductor digiti minimi in 10 cases, in the first dorsal interosseous muscle in 4 cases, and in the long flexors of the fingers in 4 cases. Owing to the nature of the job, the left hand only was affected in the majority of the men using the pneumatic hammer, the condition starting in the terminal phalanx of the little finger; in the men using the trip-hammer both hands were affected. The condition caused little disability and the use of the pneumatic hammer was not a precipitating factor, for if an attack was present it soon passed off when the men started work. Attacks were not particularly related to cold, many of the men developing attacks when their hands were warm. The condition commonly developed from 3 months to 2 years after starting this type of work and was not cured by removing the man from it. From their experimental observations the authors conclude that there are disturbances in the peripheral nerves and that these may be the main cause of the simultaneous blanching of the fingers and the motor and sensory changes.

[The incidence of Raynaud's phenomenon observed at this factory appears to be much higher than that recorded by other workers.] *L. G. Norman*

1438. **Tomography in the Radiological Study of Silicosis.** (La stratigrafia nello studio radiologico della silicosi)
E. Zanetti and A. Cardani. *Medicina del lavoro* [*Med. d. Lavoro*] **45**, 65–83, Feb., 1954. 14 figs., 37 refs.

After giving a very clear account of the value of tomography in silicotic conditions, the authors present a report on 100 cases of silicosis which were subjected to full tomographic examination at the Clinica del Lavoro Luigi Devoto, University of Milan. These cases included a variety of industrial lung diseases, and among the patients were knife-grinders, silica miners, glass workers, and others working with abrasives and similar substances. There were 8 cases of the reticular form of pneumoconiosis, 10 of the nodular form, 33 of the massive form, and in 49 cases the pneumoconiosis was associated with tuberculous lesions. The most important of their findings was the fact that in one-quarter of the cases in which the presence of tuberculosis could not be recognized on the plain film, tomography revealed the existence of tuberculous cavities. The authors describe 14 cases in greater detail and summarize their conclusions, which in general confirm those of other workers in this field.

The advantages offered by tomography are summed up as follows. (1) In the reticular type of silicosis, tomography clearly demonstrates the hilar and parahilar regions, and in particular the enlargement of the hilar lymph nodes, which is the first important feature of silicosis and in the plain film is not clearly visible. (2) In the nodular type of silicosis, tomography defines more clearly the distribution, structure, and outline of the nodules and the emphysematous areas which surround them. (3) In the nodular, confluent forms and in the massive forms tomography is of great value in identifying tumour masses, the extent of emphysema, and any deformation of the tracheo-bronchial tree. (4) In cases complicated by a coexistent tuberculous lesion tomography is invaluable for the demonstration of a cavity which is so thin that it is masked by superimposed tissues, and often enables the observer to judge from the form and structure of the surrounding tissues its likely origin. For example, when the plain radiograph shows a cavity surrounded by fibrosis and inelastic reticular tissue, tomography makes it possible to assess whether the round form of a tuberculous cavity is present, whether the form of the cavity is elongated, conical, or polyhedral due to the destruction of silicotic tissues, or whether patches of silicosis and tuberculosis coexist.

With regard to the tracheo-bronchial tree, any alteration in the size or position of the bronchi is easily observed, even when the ordinary film is quite inconclusive. The most important feature of the tomographic examination is, as stated, the early recognition of the tuberculous process and the possibility of distinguishing it either from an emphysematous bulla or from some form of emphysema surrounding an early lesion. *J. Rabinowitch*

1439. **Toxic and Fibrosing Action of Submicroscopic Particles of Amorphous Silica**
A. Policard and A. Collet. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg.*] **9**, 389–395, May, 1954. 6 figs., 12 refs.

Vapour given off when silica is exposed to intense heat condenses into a fine powder made up of particles 96% of which are smaller than 0·1 μ in diameter. Spectrographic analysis has shown this to be 99·9% pure silica and to be amorphous. In experiments at the French Collieries Study and Research Centre, Paris, and Verneuil (Oise), to assess its toxic and fibrosing effects this condensate, suspended in isotonic saline solution, was given to rats by intratracheal and intraperitoneal injection in doses of 100, 50, and 30 mg. per kg. body weight. Animals which did not die immediately were killed at intervals of 4, 8, 20, 30, and 60 days and subjected to post-mortem examination.

Intratracheal injection killed 80 to 90% of the recipient animals from acute pulmonary oedema. In the survivors collagenous pulmonary nodules developed. All the rats given 50 mg. or less by the intraperitoneal route survived. Those dying after larger doses by this route developed diarrhoea and loss of weight. In a brief account of the post-mortem examination of these animals the authors emphasize the finding of adrenal enlargement with increase of cortical lipids, which they take to indicate that the intraperitoneal injection of silica sets up a " stress reaction ". In animals which did not die immediately but were killed at intervals peritoneal oedema was observed to subside gradually; and during the period of 8 to 60 days small collagenous granulomata were seen to develop over the omentum and fibrosis to proceed in the regional lymph nodes. The lesions, both in the lungs and in the peritoneum, resembled those produced by crystalline quartz but developed more rapidly.

It is concluded that submicroscopic amorphous silica has a fibrogenic action similar to that of quartz; also that the " toxic " and " fibrogenic " actions of quartz cannot be separated, as has been suggested by some authors. *C. M. Fletcher*

Radiology

1440. **Experimental Study of the Stimulant Effect of Radiotherapy on the Adrenal Cortex.** (Étude expérimentale de la radiothérapie stimulante des cortico-surrénales)

—. THOYER-ROZAT, J. LAFARGUE, —. GILBERT-DREYFUS, J. SCHILLER, and E. A. TYAN. *Journal de radiologie, d'électrologie et Archives d'électricité médicale* [*J. Radiol. Électrol.*] **35**, 169–178, 1954. 6 figs.

In this study carried out at the Hôpital de la Charité, Paris, the adrenal areas of 96 rats were subjected to *x* irradiation at 130 kV, H.V.L. 7·4 mm. Al, through a 6-cm. layer of rice to correspond to the lumbar tissue in man (giving about 24% transmission), doses of 25, 50, or 75 r being delivered at the upper surface of the rice. The effects were assessed from changes in the weight of the glands, the blood sugar level, and the urinary nitrogen excretion, the last two being known to be controlled by 11-oxysteroids.

The results showed that gland weight was increased even after as short a period of irradiation as 45 minutes, increases in gland weight of up to 107% being found as compared with controls. The blood sugar level showed an early rise, and reached a peak in about one week. Urinary nitrogen excretion was also increased for about 18 days, whereas there was no significant increase in adrenalectomized controls. A dose of 75 r seemed to give the maximum effect possible. The main effects are attributed to the action on the cortex, since (*a*) stimulation of the medulla results in only a short period of hyperglycaemia followed by a later glycosuria, whereas the glycosuria in these experiments appeared before the maximum hyperglycaemia; and (*b*) findings similar to the above were obtained with ACTH and cortisone. The mechanism is thought to be by inhibition of utilization of glucose by 11-oxysteroids, accompanied by secondary gluconeogenesis, as shown by the increased nitrogen excretion.

In further experiments on 5 human subjects in which 100 r was delivered to the adrenal areas, increased excretion of urinary 17-ketosteroids occurred, reaching a maximum in 3 to 4 days. *J. Walter*

1441. **The Visualization of Lymph-nodes and Vessels by Ethyl Iodostearate (Angiopac) and its Effect on Lymphoid Tissue. A Preliminary Radiological and Histological Study**

H. S. BENNETT and A. A. SHIVAS. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] **5**, 261–266, April, 1954. 7 figs., 8 refs.

The contrast medium used for lymphography must be particulate, as it is the particles which are retained by the cells of the reticulo-endothelial system. The particles must be small enough, therefore, to enter the smallest lymphatics. Experiments were carried out at the Aberdeen Royal Infirmary to test the suitability for lymphography of "angiopac", which is a micronized aqueous suspension of ethyl iodostearate containing 200 mg. of combined iodine per ml.

In a preliminary experiment 10 ml. of angiopac was introduced into the peritoneal cavity of 2 rabbits, a 3rd rabbit being used as a control. Within 24 hours the medium had reached the mediastinal lymph nodes; the liver and spleen were also opacified, suggesting that the substance had entered the systemic circulation by way of the thoracic duct. The experiment was abandoned on the 6th day, up to which time the mediastinal nodes had remained uniformly opaque. There was no evidence of peritoneal irritation or general toxicity. The experiment was then repeated on 10 rats. Eight of these rats were killed at the rate of one a day and examined radiologically, the other 2 being killed and examined at the end of 6 months. In these 2 animals there was no trace of residual opacity.

On histological examination of lymph nodes visualized by this technique, necrosis, occurring chiefly as roughly circular circumscribed areas in the cortical zone, was found. High-power examination revealed complete loss of normal structure, with formation of an amorphous eosinophilic debris. The extent of necrosis was proportional to the period of exposure. In the lymph nodes from the 2 rats killed 6 months after administration of angiopac there was a complete restoration of normal architecture, though many macrophages were seen still to contain some medium.

The authors are of the opinion that there is scope for further work in the application of this technique in other regions. They further suggest that by this method direct assessment of the degree of metastatic involvement of the lymph nodes in cases of neoplastic disease might be possible; also, its possible therapeutic use in neoplastic conditions of the reticulo-endothelial system should be investigated. *John H. L. Conway-Hughes*

RADIOTHERAPY

1442. **Rodent Ulcers: an Analysis of 711 Lesions Treated by Radiotherapy**

I. CHURCHILL-DAVIDSON and E. JOHNSON. *British Medical Journal* [*Brit. med. J.*] **1**, 1465–1468, June 26, 1954. 18 refs.

The authors have analysed the results obtained with radiotherapy in all cases of rodent ulcer seen at St. Thomas's Hospital, London, during the years 1939 to 1950 inclusive, a total of 711 ulcers in 613 patients being treated. The sex incidence and the site distribution of the ulcer were in accord with those generally reported in the literature. All clinical forms were treated, excluding only those in which bone or cartilage was involved, when surgery was considered the treatment of choice. A

clinical diagnosis was considered sufficient in most cases, only 228 lesions (32%) being confirmed histologically.

Treatment was with radium or radon in 8 cases and with *x* rays of 45 to 250 kV, depending upon the estimated penetration of the ulcer, in the remainder, the majority being irradiated with a 60-kV unit. Dose fractionation depended upon the size of the area treated, and the kilovoltage used. Areas less than 2·5 cm. in diameter were given one dose of 2,000 to 3,000 r; those between 2·5 and 5 cm. were treated once or twice a week up to 3 weeks, to a total dose of 3,500 to 5,000 r; and larger areas were given 3 to 5 treatments a week for one to 3 weeks, to a total dose of 4,500 to 6,500 r.

The cure rate for all lesions treated over 3 years previously was 95·7% and for all those treated over 5 years previously was 92·6%. Of 711 ulcers, 26 recurred, of which 8 were cured by further radiotherapy, with satisfactory results. The cause of the recurrence in 9 instances was failure to irradiate a sufficient margin around the ulcer and in one the cause was inadequate dosage.

Acute radionecrosis developed in one patient for no apparent reason. Late necrosis, precipitated by trauma, infection, or sunburn, was observed in 6 cases. In only 2 cases was the dose considered slightly excessive. All necroses were treated successfully by excision or expectant measures. Cosmetic results after irradiation were good, except in those cases in which the original ulcer was large or penetrating.

[This is a valuable paper provided it is accepted that the clinical diagnosis of all rodent ulcers is both simple and reliable. The abstracter believes that histological proof is essential in many cases, and in these circumstances the absence of this confirmation in two-thirds of the authors' cases detracts considerably from the value of the paper.] *A. M. Jelliffe*

1443. **Irradiation Therapy in Hodgkin's Disease**
C. M. NICE and K. W. STENSTROM. *Radiology* [*Radiology*] **62**, 641–653, May, 1954. Bibliography.

In this report from the University of Minnesota Medical School on 224 cases of Hodgkin's disease treated by irradiation during the period 1926–48, the recent literature is reviewed and the authors' method of treatment and results are compared with those of other workers. The clinical picture and pathology of Hodgkin's disease are discussed and the neoplastic nature of the condition upheld. Negro and white subjects are equally affected, the maximum incidence being in the third decade of life. The sites of initial appearance and of subsequent involvement in the 224 cases here discussed are listed in two tables.

The authors' practice is to irradiate an entire chain of lymph nodes intensively at the first treatment. Dosage, which should be determined by the individual case, is based upon a minimum total dose of 2,000 r given over 2 weeks at 250 kV, H.V.L., 3 mm. Cu, and F.S.D. 70 cm. Higher dosage is given when there are large masses of long standing, but massive mediastinal involvement is treated by initial doses of only 50 or 75 r to obviate possible mediastinal compression, a total of 2,000 r being given in 3 weeks. Total body irradiation is occasionally given for widespread disease, and in such cases nitrogen mustard and triethylene melamine (TEM) have also proved of value, since they reduce the amount of irradiation required and produce subjective improvement; they are mainly palliative, however, and do not prolong life. Radioactive isotopes have not given comparable results. Recurrence tends to take place after surgical excision and postoperative irradiation is recommended.

The authors' results are analysed and set out in tables. The 5-, 10-, and 15-year survival rates for 208, 167, and 108 patients were 25%, 11%, and 4% respectively. Clinical staging of the disease as described by Peters (*Amer. J. Roentgenol.*, 1950, **63**, 299; *Abstracts of World Medicine*, 1950, **8**, 277) is the most accurate aid to prognosis. The 5- and 10-year survival rates for patients in Stage I were 85% and 77% respectively, for Stage II, 90% and 35% respectively, and for Stage III, 10% and 2% respectively. *G. E. Flatman*

RADIODIAGNOSIS

1444. **Controlled Pneumoencephalography. A Consideration of Head Position and Gas–Fluid Replacement**
R. SHAPIRO and F. ROBINSON. *Journal of Neurosurgery* [*J. Neurosurg.*] **11**, 122–127, March, 1954. 8 figs., 13 refs.

In this short paper from the Hospital of St. Raphael (Yale University), New Haven, the authors emphasize the advantages to be gained by carrying out controlled air encephalography as originally developed by Robertson and by Lindgren. These include: (1) precise filling of the ventricular system and basal cisterns with the minimum quantity of air, thus reducing the dangers of the procedure and causing less discomfort to the patient; and (2) low morbidity. The technique of introducing the air and the positioning of the patient are described in detail.

In the authors' experience this technique has proved far superior to the blind, relatively uncontrolled replacement of the cerebrospinal fluid with large quantities of gas. Most of the patients so far examined " had either seizure problems or craniocerebral injuries ". The authors do not advocate the routine use of this technique in patients with obvious expanding intracranial mass lesions. *W. B. D. Maile*

1445. **A New Method of Bronchography.** (Über eine neue Bronchographiemethode)
W. MAASSEN. *Tuberkulosearzt* [*Tuberkulosearzt*] **8**, 290–294, May, 1954. 3 figs., 12 refs.

In the modified technique of bronchography here described from the Sanatorium of Holsterhausen, Rhine Province, the apparatus consists of two catheters joined side by side, one being shorter than the other, so that when the lower end of the shorter catheter is at the level of the bronchial entrance into the upper pulmonary lobe, the end of the longer catheter faces the opening into the middle and lower lobes. Two occlusive balloons, each

connected by rubber tubing to a rubber bulb which acts as a pump, are attached to the catheters one above the other near their lower end. Inflation of these balloons isolates the bronchial segment situated between them so that this segment can now be filled with contrast medium through the shorter catheter without the danger of disseminating an infected sputum into other parts of the bronchial tree; for opacification of the middle and lower lobes the longer catheter is of course used. It is claimed that with this apparatus bronchography can be carried out without interruption by cough, and that alveolar filling does not occur. The author discusses the special value of this method in cases of tuberculosis.

A. Orley

1446. **Bronchographic Abnormalities in Alveolar Cell Carcinoma of the Lung. A New Diagnostic Sign**
N. ZHEUTLIN, E. C. LASSER, and L. G. RIGLER. *Diseases of the Chest* [*Dis. Chest*] **25**, 542–549, May, 1954. 5 figs., 14 refs.

The diagnosis of alveolar-cell carcinoma is difficult. There are no pathognomonic radiological signs, several diseases producing a similar picture. Bronchography has often been carried out in such cases before, but no characteristic pattern has yet been established.

The present authors have collected 6 cases of alveolar-cell carcinoma from the University of Minnesota Hospitals, Minneapolis, in all of which the diagnosis was confirmed at biopsy or necropsy. Bronchography was carried out in each case, and a peculiar bronchographic pattern was disclosed. In the involved segments the bronchi showed a uniform, diffuse narrowing, with rigidity and elongation, the terminal ramifications being free from contrast medium. This pattern is considered to be characteristic of alveolar-cell carcinoma. The authors state that they have not yet encountered an exactly similar bronchographic pattern in any other form of pulmonary disease. *D. E. Fletcher*

1447. **Involvement of the Mediastinum in Carcinoma of the Bronchus.** (Zur Frage der Mitbeteiligung des Mediastinums beim Bronchialkarzinom)
F. STRNAD. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **80**, 427–438, April, 1954. 14 figs., 7 refs.

With the recent increase in the number of operations for pulmonary neoplasm it has become still more important to obtain adequate information about the extension of a growth into the mediastinum, and also about its possible fixation to the organs therein. The author, working at the University Surgical Clinic, Frankfurt am Main, conjectured that it should be possible to outline the oesophagus with barium and then by kymography to note whether there was normal transmission of pulsation from the cardiac chambers. In the normal subject the pulsation serration observed in the oesophageal outline extends the length of the anterior or posterior cardiac wall and is very easily demonstrable. This serration is maximal at the level of the auricle and ventricles, and only decreases considerably higher up in the mediastinum, especially at the level of the aortic impression and at the bifurcation. If a pathological process were present in the mediastinum there would be a smoothing of the serration pattern, suggesting that the oesophagus was fixed and incapable of full free movement in the mediastinum.

The author therefore tested this contention by examining over 100 patients, including cases of bronchial carcinoma, hilar-node lesions, oesophageal growths, inflammatory disease of the lungs, and a few post-operative cases in which a bronchial neoplasm had been removed. From the degree of reduction of the pulsation amplitude it was possible to determine the extent of the growth process. He found, for example, that a benign neoplasm did not cause any reduction of the pulsation pattern, and that a normal serration picture was obtained in cases of Boeck's sarcoid involving the mediastinum and in cases of mediastinal encysted empyema, pleurisy, and inflammatory lung disease. Complete absence of a transmitted pulsation pattern was taken to indicate that the oesophagus was completely enveloped by the neoplasm and that the case was inoperable. Of 53 cases so examined and which later came to operation, his prediction as to the location of the growth and the degree of involvement was found to be correct in 50 cases. While this examination in itself does not permit of an absolute decision as to whether a growth is operable or not, it can certainly serve as an indication of what complications or difficulties are likely to be encountered at operation. *J. Rabinowitch*

1448. **Angiopneumography in the Study of the Pharmacodynamic Properties of Certain Drugs**
L. DE CARVALHO. *Diseases of the Chest* [*Dis. Chest*] **25**, 121–127, Feb., 1954. 5 figs., 1 ref.

The pharmacodynamic effect of certain drugs on the pulmonary circulation was investigated at the Santa Marta Hospital, Lisbon. By using the technique of angiopneumography the author was able to demonstrate the marked slowing of the pulmonary circulation which occurs after intravenous injection of adrenaline, posterior pituitary extract (" pituitrin "), or *iso*nicotinic acid.

An intravenous injection of 3 ml. of thorotrast was given to rabbits, and serial angiographs were taken at varying intervals. Serial angiographs were then taken after intravenous injection of: (1) 0·5 ml. of a 1-in-1,000 solution of adrenaline; (2) pituitrin [dose not stated]; and (3) a solution containing 0·1 g. of *iso*nicotinic acid. It was found that pituitrin had the most prolonged and retarding effect on the pulmonary circulation. [This paper is well illustrated.] *B. Green*

1449. **Transversoaxial Tomography as a Valuable Help in Estimation of Operability of Pulmonary Cancer**
E. FORSTER, D. SICHEL, and E. ROEGEL. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **27**, 593–602, June, 1954. 6 figs., 7 refs.

Horizontal tomography has been most used in France and Italy, and in this paper from Strasbourg the authors discuss its value, in cases of pulmonary carcinoma, in demonstrating the extent of involvement of the mediastinum and pulmonary veins—that is, whether there is

a plane of cleavage between the pulmonary tumour and the mediastinal structures—and hence the operability of the growth. The demonstration of a plane of cleavage depends to a large extent on the anatomical disposition of the structures. In horizontal tomography the trachea, oesophagus, superior and inferior vena cava, and the right border of the heart are sectioned perpendicularly to their axes, and appear clearly outlined. The appearances in the left side of the chest are often more difficult to identify, because the curved left border of the heart and the oblique arch of the aorta mask the pulmonary artery, obscuring the limits of these organs on the horizontal tomogram and confusing the outlines of the tumour.

The authors state that they have used transverso-axial tomography for over one year in all cases of pulmonary carcinoma. Three cases are briefly presented, with reproductions of frontal, lateral, and horizontal tomograms.

[The reproductions are poor in quality. The use of this method of investigation is limited by the cost of the apparatus required.] *Sydney J. Hinds*

1450. **The Technique of Angiocardiography.** (Методика ангиокардиографии. Сообщение I)
E. N. MESHALKIN. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **32**, 21–30, Feb., 1954. 2 figs.

In the surgical treatment of heart disease accuracy in diagnosis is essential, and for this an exact knowledge of the anatomical structure and function of the heart and great vessels is of prime importance. This necessitates investigation of the pressure, oxygen content, saturation, and course of the blood, both in the chambers of the heart and in the great vessels, and this involves the use of the cardiac cathether and of contrast media. The effect of these methods on the function of the heart and and on the patient as a whole requires careful investigation.

The author describes his technique, which resembles that generally used except that he has frequently employed retrograde catheterization from the arterial side and finds this approach of much value and likely to cause fewer complications than the venous approach. Of 60 instances of cardiac catheterization, 49 were performed intravenously and 11 intra-arterially. In 42 of the former and all 11 of the latter, no serious disturbances of cardiac rhythm resulted, although of 39 other cases examined by the intravenous route with simultaneous electrocardiography, 22 showed some disturbance of action, extrasystoles occurring in 7 cases as the catheter passed into one or other of the heart cavities. There were no disturbances of arterial pressure, pulse, or respiratory rate. Complications, which occurred in 9 cases examined intravenously, included 4 cases of transverse rupture of the vein, one of detachment of the directing nozzle of the catheter, one of difficulty in withdrawal, and 3 of blood clot in the catheter; among the patients examined intra-arterially there were 2 cases of transverse rupture of the artery, in both of which, however, the artery was successfully sutured and circulation in the arm fully restored.

A total of 185 injections of contrast material (120 of "cardiotrast" and 65 of "pyelosil" (diodone)) were given, 163 by the intravenous route (50 by catheter, and 113 directly into the vein) and 22 by the arterial route, all by catheter. The reactions produced by the introduction of contrast material into the circulation depended not only on the amount of contrast material per kg. body weight of the patient, but also on the rate of injection, and the author suggests a "weight–time coefficient" based on the formula:

$$\text{Weight–time coefficient} = \frac{\text{weight of dry medium in g.}}{\text{weight of patient in kg.} \times \text{duration of injection in seconds}}$$

The author found that if this coefficient exceeded 0·3, reactions were liable to be severe, and if above 0·7, very severe. Symptoms included a feeling of oppression in the chest, nausea, vomiting, pallor, cyanosis, in most cases hyperaemia of the skin, and in 24 cases urticaria. Children with congenital heart disease were especially susceptible if the weight–time coefficient exceeded 0·4. In tests on experimental animals, a severe fall in the arterial pressure occurred when the coefficient was higher than 0·45.

The introduction of the cardiac catheter and also the avoidance of severe reactions to contrast material is much facilitated by preliminary intravenous injection of procaine. In the author's experience angiocardiography is dangerous in patients with disturbances of conduction, hypoxia of the myocardium or general hypoxia associated with congenital morbus cordis, or renal insufficiency, and in patients sensitive to iodine.

L. Firman-Edwards

1451. **Myelography in Spinal Metastases**
S. HEISER and A. J. SWYER. *Radiology* [*Radiology*] **62**, 695–702, May, 1954. 6 figs., 19 refs.

During a recent 5-year period at the Montefiore Hospital, New York, a total of 75 tumours involving the spinal canal were studied by myelography. Of these tumours 20 proved to be due to metastatic deposits and 6 were lymphomata. These figures are higher than those reported by other workers

The mechanism of metastatic spread to the spinal cord is discussed in detail. The primary site of the tumour in 8 of the 20 cases of metastatic carcinoma was the lung (5) and the breast (3). The lymphomata were distributed equally in the spinal lumbar and dorsal areas.

Routine *x*-ray examination of the spine disclosed evidence of metastases in 12 of the 20 cases, and in 10 of these the level of cord compression coincided with that determined clinically. The interpediculate measurements were not considered to help in the diagnosis of metastatic bone involvement, evidence of erosion or destruction of the roots of the neural arches being of more value. There was no evidence of calcification and no paravertebral soft-tissue masses were observed. The myelographic appearances varied considerably, no specific pattern being identified; even the differentiation of intradural and extradural lesions was difficult.

The authors consider that myelography should be carried out at once when there is clinical evidence of

cord compression, even if a primary neoplasm is known to be present, since in many cases routine radiographs of the spine fail to reveal bone changes.

W. B. D. Maile

1452. **A Contribution to the Radiological Study of the Postoperative Peptic Ulcer. The Diagnostic Value of Changes in the Calibre of the Ulcerated Loop (Stenosis and Bursiform Dilatation).** (Contribution à l'étude radiologique de l'ulcère peptique post-opératoire. La valeur diagnostique des modifications de calibre de l'anse ulcérée (rétrécissement et dilatations bursiformes))

L. LAMBLING and A. GUÉRET. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. Appar. dig.*] **43**, 273–284, March, 1954. 8 figs., 5 refs.

The authors, writing from the Hôpital Bichat, Paris, recall that the demonstration of a niche has been regarded as the primary sign of a postoperative gastro-duodenal or jejunal ulcer, but point out that in many cases where no niche has been seen an ulcer crater has later been found at laparotomy. They have therefore sought to establish secondary signs of ulceration in this area.

They recommend that the radiological search should be made with the patient in the erect position and the stomach full, followed if necessary by the more usual method with the patient prone or supine. In cases of postoperative ulcer they have found that a most significant sign is a diminution in the calibre of the jejunum of varying extent, associated with a bursiform dilatation which may be single or double, and which, if double, often encircles the narrowed zone of the jejunum. Concentration of observation on this narrowed zone may facilitate the search for an ulcer within it, or in the immediate neighbourhood. It also allows the identification as ulcers of doubtful shadows appearing within the narrowed zone. At the least, this narrowing of the jejunum is strongly suggestive of the presence of an ulcer, even in the absence of a niche, and in the authors' opinion when this characteristic appearance is seen and is accompanied by pain or haemorrhage, laparotomy is justified. *John H. L. Conway-Hughes*

1453. **The Place of Intravenous Cholangiography in the Diagnosis of Diseases of the Biliary Tract.** (La place de l'angiocholégraphie intraveineuse dans le diagnostic des affections de la voie biliaire principale)

J. CAROLI, P. PORCHER, E. GILLES, J. LEDOUX, and —. CHARPENTIER. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. Appar. dig.*] **43**, 285–304, March, 1954. 12 figs.

In the last 6 months the authors have examined 110 cases of liver or biliary tract disease by means of intravenous cholangiography and in a retrospective review of these cases they have endeavoured to determine to what extent this method of examination has superseded previous methods of investigation of these disorders. Problems of technique are not discussed, it being assumed that every care is taken to obtain satisfactory films. In cases of jaundice or when the serum bilirubin level is above 2 or 4 mg. per 100 ml. cholangiography is not likely to be successful. If the "bromsulphalein" test is normal a good result from cholangiography may be expected; if the retention of bromsulphalein at 45 minutes is less than 20% a fairly good result may still be obtained, but its appearance is likely to be delayed; if the retention reaches the level of 30%, cholangiography is not likely to be satisfactory. The bromsulphalein test ought therefore to serve as a guide to the use of "biligrafin". The use of this substance is not recommended in cases of suspected hepatic jaundice owing to the risk of reaction, but it may be used when there is a temporary recession in the jaundice and the retention of bromsulphalein is not above 20% at 45 minutes.

Investigation by cholangiography is probably of greatest value after cholecystectomy, and it is in these cases that the best visualization of the common duct is obtained. The duct, which should show no marked segmentation, should be visualized immediately, as should also its junction with the second part of the duodenum; but opacification should not persist for more than 2 hours and should disappear rapidly after a fatty meal. The stump of the cystic duct is usually also clearly seen, and should not appear dilated. If there is spasm or narrowing at the sphincter of Oddi the duct may still be visualized at 3 hours and opacification does not disappear after a fatty meal, while the stump of the cystic duct is usually dilated.

Cholangiography is a helpful diagnostic procedure in practically every disorder of the biliary tract even when, as in many cases, an ordinary cholecystogram has given no information. *John H. L. Conway-Hughes*

1454. **Roentgenographic Demonstration of Histologically Identifiable Renal Calcification**

J. MORTENSEN, A. H. BAGGENSTOSS, M. H. POWER, and D. G. PUGH. *Radiology* [*Radiology*] **62**, 703–712, May, 1954. 4 figs., 6 refs.

At the Mayo Clinic the deposition of calcium in the renal parenchyma was studied. It is pointed out that calcium is frequently found on histological examination of kidneys which have functioned normally, but that it is rarely seen on radiographs. The radiological demonstration of deposits of calcium in the kidneys is of considerable clinical importance.

Radiographs of one or both kidneys were taken post mortem in 210 histologically proven cases of renal parenchymal calcification. In only 6 of these was multiple diffuse parenchymal calcification identified. In a further 30 cases there was calcification due to isolated pathological lesions such as cysts, neoplasms, infarcts, calcified renal vessels, or calculi.

The authors deduce from their preliminary studies that although the quantity of calcium present in renal tissue, as determined by quantitative chemical analysis, appears to be directly related to the ability of that tissue to cast recognizable shadows, neither gross nor histological estimations of the size, number, density, or extent of renal calcifications "are reliable indications of the radiographic demonstrability". They add that it is not clear why calcification is visualized in some cases and not in others, but that the quantitative chemical deter-

minations in general indicate that there is a higher content of calcium in those kidneys with radiologically demonstrable deposits than in those without. They consider that radiology is a practical method of separating a small group of cases with a certain degree of calcification from the large group in which calcification is only demonstrable histologically, and that the condition in the former group should be termed " nephrocalcinosis ".

W. B. D. Maile

1455. **Intraosseous Venography of the Lower Limb and Pelvis**

A. C. BEGG. *British Journal of Radiology* [*Brit. J. Radiol.*] **27**, 318–324, June, 1954. 20 figs., 6 refs.

The author describes a new method of venography in which the contrast medium is injected by the intraosseous route; this method he has now employed at Dunedin Hospital (Otago Medical School), New Zealand, in the examination of 30 patients without untoward incident. The technique is as follows. Some 15 minutes before the examination, 1,000,000 units of penicillin is administered (though this is probably unnecessary) and the patient then lies supine on the *x*-ray table. Anaesthesia by means of intravenous thiopentone is induced, and the skin is punctured aseptically with a Kirschner wire. Through the puncture hole a special needle, 1·2 mm. in internal diameter and 6 cm. long, is introduced and pushed through the cortex into the bone marrow. After the withdrawal of the stylet a syringe is attached to the needle and negative pressure being applied, blood usually flows back freely into the syringe; if it does not, the needle is introduced a little further until it does. A syringe containing 20 ml. of 50% " uriodone " is fitted to the needle, the injection is made rapidly in 3 to 5 seconds, and an antero-posterior film exposed immediately. The syringe is left attached to the needle while the film is processed and during this time the plunger is pushed back by the intramedullary pressure until 5 or 10 ml. of blood is collected. A further injection may be made if desired; the needle is then withdrawn and a dressing applied firmly.

The selection of the site of injection depends upon the particular problem involved. To demonstrate the pelvic veins, the internal iliac vein, the common iliac vein, and the inferior vena cava the great trochanter has proved to be the most suitable site, while injection into the tibial tuberosity has been found most satisfactory for demonstration of the superficial and deep veins of the thigh and of the external iliac vein; the veins of the thigh can be visualized at the end of the injection and those of the pelvis 3 seconds later. To show the venous systems of the leg and thigh, the lower end of the tibia is the best site, but if this is covered by an ulcerated area, the lower end of the fibula may be used. The veins of the leg will be shown immediately at the end of the injection with the leg in slight external rotation, while those of the thigh are visualized 5 seconds later. Improved filling of the thigh veins is obtained by raising the limb through 45 degrees as soon as the film of the leg has been taken, then lowering it and exposing the film of the thigh immediately.

In the author's experience intraosseous venography provides a safe, simple, flexible, and certain way of demonstrating the deep venous system of the leg and pelvis. It allows of the demonstration of the communicating veins between the superficial and deep systems and clearly shows the retrograde flow which occurs when they become incompetent; it also gives an excellent demonstration of the anastomotic circulation which is developed after venous thrombosis. Injection of the medium has presented no difficulty, no matter how oedematous the leg may be or how poor the superficial venous system.

L. G. Blair

1456. **Radioactive Gallium as a Test for Malignant Tumours of Bone.** (Le test au 72 gallium dans les tumeurs malignes des os)

H. DESGREZ, R. A. GUÉRIN, and M. T. GUÉRIN. *Presse médicale* [*Presse méd.*] **62**, 997–998, June 26, 1954. 15 refs.

Radioactive gallium (^{72}Ga), which has a half-life of 14·1 hours, is selectively concentrated in osseous tissue. In normal bone the maximum uptake is reached in one hour, but in the presence of deranged osteoblastic activity the uptake is more gradual and is prolonged over a period of 10 hours. In the test described, which was carried out by the authors in 17 cases of tumour of bone, 0·4 to 1·0 millicurie of ^{72}Ga was administered orally in the form of 100 mg. of gallium nitrate. Radioactivity was measured 24 and 48 hours later, after an enema had been given to remove any gallium from the bowel. The Geiger–Müller counter remained fixed at a distance of 25 cm. above the patient, the latter being moved in such a way that the counting rates over symmetrical areas of the skeleton could be compared; an increase of less than 20% was not considered to be abnormal. The preliminary measurements were made with a collimator having an aperture 35 mm. in diameter, but selected areas were subsequently scanned in greater detail using a collimator with an aperture of 8 mm., thus enabling small islands of increased activity to be detected.

There was a significant increase in the counting rate (from 20 to 400%) over the affected areas in 9 patients with malignant involvement of bone, comprising cases of osteogenic sarcoma, Ewing's tumour, and secondary deposits from tumours of the breast, lung, kidney, and prostate, and also in one further case with bone involvement due to myeloid leukaemia. In some cases the radioactivity measurements showed more extensive involvement than that demonstrated radiologically. Serial tests with ^{72}Ga also appeared to be useful in assessing the response of lesions to radiotherapy.

As a control, the same test was carried out in 7 cases of non-malignant involvement of bone, comprising cases of benign osteoma, localized cortical thickening, osteitis condensans ilii, Paget's disease, and chronic inflammatory lesions. In 6 of these patients, the concentration of ^{72}Ga was normal. In one patient with a subperiosteal haematoma there was a localized area of increased activity of 30%, but biopsy examination revealed only inflammatory changes.

G. Ansell

History of Medicine

1457. **An Experiment of Galen's Repeated**
J. M. FORRESTER. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **47**, 241–244, April, 1954. 21 refs.

The author first reviews the rival Galenic and Erasistratean theories on the nature of pneuma (which was thought to fill the arteries) and of bleeding, and discusses the views of Harvey, who also repeated Galen's experiment in 1649 in the course of his further studies of the circulation. The experiment referred to is one which Galen performed about 170 A.D. in an attempt to refute the views of the followers of Erasistratus regarding the nature of bleeding and the cause of pulsation of arteries. It involved the opening of an artery of a living animal and the insertion of a hollow metal tube or reed into its lumen. When the artery was then firmly tied about the tube Galen found that pulsation in the artery distal to the ligature was stopped, thus confirming his view that pulsation was caused by a " power " transmitted from the heart along the walls of the arteries.

Recently at the University of Oxford the present author repeated this experiment as closely as possible in an attempt to reproduce Galen's anomalous finding, which he was, however, unable to do, the distal part of the artery continuing to pulsate as before. No final opinion as to the cause of Galen's unexpected result is expressed, but several hypotheses are examined.

Calvin P. B. Wells

1458. **Remains of Medieval Hospitals in the Île-de-France North of Paris.** (Les hôpitaux du moyen âge en Île-de-France. Leurs vestiges au nord de Paris)
P. VALLERY-RADOT. *Presse médicale* [*Presse méd.*] **62**, 1051–1052, July 7, 1954. 3 figs.

The Île-de-France, formerly a province, is the name now given to that region north of Paris bounded by the rivers Seine, Marne, Beuvronne, Thève, and Oise, and within this area may still be found the buildings which housed ten hospitals built in the Middle Ages. In this short paper the author briefly describes five of these. The Hôtel Dieu de Gonesse, 12 miles from Paris, was built in the late 13th century and was used as a home for the aged until about a century ago, when the present Hôtel Dieu was built on a site opposite. Near Senlis is the Hôtel Dieu de Gollande, which was founded in 1170 by Louis le Jeune and thereafter remained under the patronage of the kings of France; to this day, in spite of its present use as a workshop and woodstore, it is still a fine example of Gothic architecture. Further north, at Compiègne, is another 13th century hospital famous for its tiercepoint windows and its magnificent main hall measuring 60 metres by 17.

The author considers, however, that the most beautiful of all these medieval hospitals is that of the abbey of Ourscamp, some 90 kilometres from Paris, which was built about 1240 and has miraculously survived a revolution and many wars. It is in excellent condition and is now used as a chapel; there is also an adjoining room which is presumed to have served as a dispensary. The hall itself is 30 metres long and could hold four rows of twenty-five beds each. The beautiful vaulted roof is supported on two rows of fine, slim columns. Since the building was quite separate from the nearby abbey it may have been used as a mortuary for victims of the plague, and this would explain its colloquial name of *salle des morts*.

F. Clifford Rose

1459. **François Rabelais, Physician. The Influence of Medicine on His Work.** (François Rabelais, médecin. Influence de la médecine sur son œuvre)
J. MARGAROT. *Biologie médicale* [*Biol. méd.*] **43**, 3–62, June, 1954. 28 figs.

The fame of François Rabelais (*c.* 1494–1553) rests of course mainly on his work as a writer and satirist. It is less well known that during the latter part of his life he was a practising physician. In this article, written from the Faculty of Medicine, Montpellier, on the occasion of the fourth centenary of Rabelais's death in 1553, an assessment is made of his medical knowledge and practice, and of the influence of medicine on his literary work.

It was as a monk and lay priest pursuing humanistic studies that Rabelais first gained some of his earliest medical knowledge, but it was not until 1530, when he was already nearly forty, that he matriculated as a medical student at the University of Montpellier. His approach to medicine was that of the humanist, seeking a return to the literal texts of the ancients, but applying to their teaching his remarkable critical ability. An example of his work in this field was his translation of the *Aphorisms* of Hippocrates, which was published at Lyons in 1543. In an estimate of Rabelais's medical knowledge and original thought the author shows that his subject is worthy of comparison with his famous contemporaries, Vesalius, Ambroise Paré, and Jean Fernel. (Reproductions of portraits of these and of other famous men of the period, as well as of interesting documents from the library of the Faculty of Medicine of Montpellier, illustrate the article.)

Less is known of Rabelais's methods of practice, but he favoured the Hippocratic principle of cheerful and cooperative treatment of the patient. His wandering life precluded the formation of a large practice, but the fact that he had among his patients such eminent men as Cardinal du Bellay, whom he accompanied to Rome, and the tributes of his contemporaries show that Rabelais was held in high esteem as a physician. Medical references abound in the bewildering complexity of his literary works, but the precise influence of medicine on their composition is hard to determine. *Gargantua* and *Pantagruel* were possibly written for the amusement of patients;

the fact that they were published during the last twenty years of their author's life might indicate that they were Rabelais's form of light and extravagant relief from the strain of medical practice. The often marked crudity of language may have had its origin in medical terminology, and the shrewd characterization have been the result of those opportunities for observation which are afforded to a medical practitioner. Above all, the frequent and correct use of medical terms, and the descriptions of abnormalities and other conditions of medical interest, confirm that the author of these works was indeed a professional physician. *F. M. Sutherland*

1460. **Josiah Wedgwood, Medallions, and Physicians**
H. H. FERTIG. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **28**, 127–139, March–April, 1954. 10 figs., 7 refs.

Josiah Wedgwood, the famous eighteenth-century English potter, was well acquainted with a number of outstanding physicians of his day, and produced some ceramic ware which is of particular interest to the medical profession. He is best known to some for his jasper ware, and the majority of his portrait medallions, which were generally cut in profile, were made in white jasper on a blue ground. Wedgwood's sixth catalogue contains a group entitled " Heads of Illustrious Moderns ", representing the most famous figures from Chaucer's time (1400) to the end of Wedgwood's life in 1795. In this group 10 physicians are listed, but actually medallions of 25 physicians were produced, the others being listed elsewhere since their chief claim to fame lay outside medicine. The 10 physicians include William Buchan, who wrote *Domestic Medicine, or the Family Physician*, " the first home English medical adviser "; the Dutch clinician and teacher Hermann Boerhaave; and Erasmus Darwin, scientist and physician, who, like Wedgwood, was a grandfather of Charles Darwin. Also portrayed are the physiologist Albrecht von Haller, Sir Hans Sloane, Richard Mead, Henry Pemberton, John Fothergill, Gerhardt van Swieten, and John Freind. Physicians listed as philosophers and naturalists include Sir George Baker, famous for his *Essay concerning the cause of the endemic colic of Devonshire*; Linnaeus, the botanist; John Locke, the philosopher; and the Scottish chemist, John Black. Strangely enough, Wedgwood did not make a medallion of William Withering, whom he knew well, and it is difficult to account for this omission. [The article is well illustrated and contains reproductions of the 10 medallions.] *Ruth Hodgkinson*

1461. **James Syme (1799–1870)**
J. M. GRAHAM. *British Journal of Plastic Surgery* [*Brit. J. plast. Surg.*] **7**, 1–12, April, 1954. 5 figs.

James Syme was born in a house in Princes Street, Edinburgh, opposite the place where the Scott Memorial now stands. He was educated at the High School, the buildings of which were eventually taken over by the Royal Infirmary and adapted as the Surgical Hospital, to which Syme went as Regius Professor of Surgery, and where he was followed by Lister. Syme attended the Faculty of Arts at the University before he took up the study of medicine, and during this period he discovered the method of waterproofing textiles, which now bears the name of Macintosh. Syme stated that the only profit he gained from the discovery was the confidence he acquired in solving a difficult problem. He became friendly with Liston through attending his extramural class on anatomy, and succeeded him as lecturer at the age of 23; after 3 years, however, he gave up anatomy to lecture on surgery. This made him a rival of Liston, and brought about an estrangement which was not healed until the latter was appointed to the chair of Surgery at University College, London.

Syme's courage and determination are revealed by his performance at the age of 24 of the first operation in Scotland for amputation through the hip. At 29 he had a resounding surgical reputation, and would have been appointed to the staff of the Royal Infirmary had the managers not feared that the rivalry with Liston would lead to scenes. Syme therefore established his own hospital in Minto House, not far from the University. For 4 years he steadily increased his reputation at home and abroad; during this period he wrote his *Principles of Surgery*.

In 1833, when James Russell, the first Regius Professor of Surgery in Edinburgh, retired, Syme was appointed to the chair on his merits as a teacher and because he agreed to pay the retiring professor a pension of £300 a year, a usual arrangement in those days but one which Liston refused to countenance. A little known incident in Syme's life is his acceptance of the chair at University College after Liston's death in 1847; he remained there only 5 months, and then, the chair at Edinburgh still being vacant, he returned, receiving a very cordial welcome. Here as Professor of Surgery he perfected his method of clinical teaching by the demonstration of cases before the whole class. Dr. Joseph Bell (whose methods of observation and deduction had suggested the character of Sherlock Holmes to Conan Doyle) stated that Syme's operating " was devoid of flourish and dash. He was not very rapid and not very elegant . . . He thought of nothing but the patient and the best—not the most rapid, not the showiest, not the easiest—but the best way of relieving him. His imperturbable coolness was contagious, and he was generally well assisted ".

Syme's contributions to surgery were many. His first, at the age of 22, was the description of periosteal bony hypertrophy in the vicinity of a chronic ulcer. He developed, in the days before anaesthesia, external urethrotomy for stricture, recording 109 cases. His method of amputation at the ankle carried a lower mortality (for those days) than amputations higher up. He successfully performed the Hunterian operation for aneurysm in 34 out of 35 cases. His most dramatic case was one in which he excised an enormous tumour of the jaw from a young man of 24, who survived the procedure and 17 years later, on returning from America, encountered Syme in Princes Street, to their mutual satisfaction. In 1857 Syme devised an operation for removal of the whole of the tongue, being the first surgeon to accomplish this; the first two operations were failures, but the third, performed in 1865, was successful. He was familiar with the methods for

restoring the nose by pedicle flaps from the cheek and forearm, and devised a technique for closing the gap left after excision of the whole of the lower lip.

Syme's name will always be linked with that of Lister, for Lister, at the age of 27, became his house surgeon and subsequently, in 1856, married his daughter Agnes. In this year he was appointed assistant surgeon to the Royal Infirmary, where he remained until he went to Glasgow in 1860. Syme's career ended in 1869, when he suffered a left-sided hemiplegia and resigned his chair to Lister. It was typical of his alert and vigorous mind that he was one of the first to champion Listerian principles. *J. G. Bonnin*

1462. **Glasgow's Place in the Distinction between Typhoid and Typhus Fevers**
A. L. GOODALL. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **28**, 140–153, March–April, 1954. 1 fig., 48 refs.

Epidemics of typhus fever were frequent in the early nineteenth century in Glasgow, and the town became one of the centres to which European workers travelled to study the disease. At the same time typhoid fever was endemic in the district. Glasgow had recently become industrialized and the demand for labour had attracted a large number of Irish workers, whose living conditions were appalling. It is not surprising therefore that Glasgow is mentioned frequently in papers on the continued fevers.

From the earliest times many authors had described a continued fever differing from typhus; Hippocrates in his *Epidemics* describes 2 cases which may well have been what is now known as typhoid. Among later writers Pringle in 1750 distinguished two types of continued fever, and an epidemic of what must have been typhoid is described by Ebenezer Gilchrist of Dumfries in 1734. In the following century many accounts of this type of fever appeared, among them one by James Muir, who in 1812 reported a limited outbreak at Paisley, 7 miles from Glasgow. Up to this time, however, no one had stated categorically that there were two distinct diseases, different in aetiology, symptomatology, and prognosis.

In 1836 Robert Perry, a physician at Glasgow Royal Infirmary and Fever Hospital, published a paper on continued fevers in which he correctly described many of the distinctions between the two types. He put forward 14 propositions which were based on upwards of 4,000 cases and 300 necropsies. Among these was the statement that it was rare to find disease of the mucous membranes of the intestines in cases of typhus fever, and another that inflammation of the lymphoid tissue of the intestines is a disease *per se* and capable of being distinguished from typhus by a number of clinical features which he described. A. P. Stewart, another graduate of Glasgow, further clarified the distinction between the two fevers in a paper to the Medical Society of Paris in 1840. Other important contributions were made by Peebles, Anderson, and Ritchie, all of Glasgow, but to Perry must go the credit of first distinguishing between typhus and typhoid fevers, although at the time of the publication of his paper Gerhard and Pennock were already independently collecting similar evidence in the U.S.A. *Ruth Hodgkinson*

1463. **Hallopeau's Communications on Lichen Sclerosus et Atrophicus**
E. GAHAN. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **69**, 435–437, April, 1954. 10 refs.

1464. **Cox and Trotter, Two Psychiatric Precursors of Benjamin Rush**
W. OVERHOLSER. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **110**, 825–830, May, 1954. 2 figs., 6 refs.

1465. **A Forgotten Psychiatrist—Baron Ernst von Feuchtersleben, M.D., 1833**
C. L. C. BURNS. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **47**, 190–194, March, 1954.

1466. **Carl Adolph von Basedow. The Centenary of his Death.** (Carl Adolph von Basedow. Zu seinem 100. Todestage)
L. BUCHHEIM. *Endokrinologie* [*Endokrinologie*] **31**, 129–133, April, 1954. 1 fig.

1467. **Dr. Edward Wilson of the Antarctic. A Biographical Sketch, Followed by an Inquiry into the Nature of His Last Illness**
B. J. FREEDMAN. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **47**, 183–189, March, 1954. 2 figs., 6 refs.

1468. **Pre-Columbian Ceramic Vases of the Ancient Nazca Culture, Showing Possible Gummata of the Leg**
P. WEISS and L. GOLDMAN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 145–147, March, 1954. 1 fig., 6 refs.

1469. **The History of the Spread of Syphilis in Africa from Contemporary Travellers' Records.** (Die Geschichte der Verbreitung der Syphilis in Afrika nach zeitgenossischen Reiseberichten)
A. SPRINGER. *Hautarzt* [*Hautarzt*] **5**, 227–233, May, 1954. Bibliography.

1470. **Medical Chemistry and " the Paracelsians "**
R. MULTHAUF. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **28**, 101–126, March–April, 1954. Bibliography.

1471. **The Artist as Physician. Medical Philosophy in the Renaissance**
F. MARTÍ-IBÁÑEZ. *International Record of Medicine* [*Int. Rec. Med.*] **167**, 221–242, April, 1954. 9 figs., 1 ref.

1472. **The Manuscripts of Morgagni's " Laurenziani," Known but Neglected.** (I manoscritti " Laurenziani " di G. B. Morgagni, noti, ma ignorati)
A. PAZZINI. *Rivista di storia delle scienze mediche e naturali* [*Riv. Storia Sci. med. nat.*] **44**, 165–186, May–Dec., 1953. 45 refs.